HUMANE CARE AND DEVELOPMENT OF SUBSTITUTES FOR ANIMALS IN RESEARCH ACT

HEARING

BEFORE THE

SUBCOMMITTEE ON
SCIENCE, RESEARCH AND TECHNOLOGY

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES

NINETY-SEVENTH CONGRESS

SECOND SESSION

ON

H.R. 6245

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HUMANE CARE AND DEVELOPMENT OF SUBSTITUTES FOR ANIMALS IN RESEARCH ACT

TUESDAY, MAY 4, 1982

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY,
Washington, D.C.

The subcommittee met, pursuant to call, at 9 a.m., in room 2318, Rayburn House Office Building, Hon. Doug Walgren (chairman of the subcommittee) presiding.

Present: Representatives Walgren, Weber, Shamansky, and Skeen.

Mr. WALGREN. I want to welcome you all to the hearing today. Last fall our subcommittee began the process of trying to put in legislative form some of the many concerns of the animal welfare and scientific research communities with respect to laboratory animal treatment. It seemed to us that this was certainly a most important area where the values and the needs of science meet broader values and concerns of society as a whole. I believe that this meeting point does not have to represent a distrustful clash but rather it can be an opportunity for each community involved to reach for and achieve a broader understanding of the other.

It was for that reason that we began last January, to circulate a draft subcommittee bill on this subject and I want to express my appreciation to other Members of Congress for their interest in this area; particularly the chairman of the full committee, Mr. Fuqua, and Mrs. Schroeder, Mr. Lantos, and subcommittee colleagues, Mrs. Heckler, Mr. Brown, Mr. Hollenbeck, and Mr. Roe for their particular interest and their suggestions. We are also particularly grateful to many of the citizens in the research and animal welfare communities who have participated in discussions and given us a great deal of helpful information through written materials and written commentary. It seems to me that the material that we did receive in writing in response to this process is extremely valuable and we will include certainly a portion of that in the hearing record as we go along, so that there will be a very broad record from which to consider this matter.

It is clear that no matter what we do the legislation will obviously not be perfect and will not have unanimous support. The record of the commentary we received on the draft bill, however, may provide us with a direction in which we may find some improvement and we would want to consider that among the members of the subcommittee as we go along.

The hearing today will complete the formal process and we will be listening closely to the suggestions of Government agency colleagues on how to improve the product that is now represented in H.R. 6245.

As most of you know, the legislation has four basic parts. It places special emphasis on the development of research and testing methods which could reduce the number of animals used in research and testing or certainly minimize animal pain and distress.

It would require a rigorous standard for accreditation of Federal laboratories and federally funded research institutions which use animals in research or testing.

It attempts to insure the participation of community representatives and veterinarians on animal care committees at research institutions and requires that these local committees review both animal care facilities and research protocols for compliance with accepted standards of treatment and care.

It also requires scientific peer reviev panels to evaluate the importance of proposed scientific findings as balanced against the animal distress which may be involved in the experiments that they are considering funding.

Of course, the current product has not met all the concerns of many interests. There is still room for adjustment. We are still open. We will be listening to the suggestions received today, as well as those of congressional, research and animal welfare communities to come up with a package of amendments which we hope will strengthen the bill and that both Mrs. Heckler, the ranking minority member, and myself could support.

In the end, I hope that the many people that have been involved in these groups will be able to give this legislation their support. At the beginning of the process, conventional wisdom was that this issued involved feelings that were too strongly held to allow any ordinary compromise and for that reason was not really a constructive area for legislative process.

Though there have been many bills introduced in recent years it was thought as a practical matter, not very possible to move any of them through the hurdles of legislation.

I hope that we will prove that conventional wisdom wrong. I think that we can complete the job of developing legislation that meets most of the concerns of the animal welfare advocates, and not only allows, but actually facilitates the progress of significant areas of science where animal experimentation is crucial. Providing an institutional framewok for laboratory animal protection in which the public can have confidence is the best way to insure that important research is not disrupted by controversy over breaches of standards of care that may violate public sensitivity.

We appreciate very much the witnesses coming today and I would be happy to recognize and welcome Mr. Weber.

Mr. WEBER. No statement, Mr. Chairman, thank you.

STATEMENT OF WILLIAM F. RAUB, ASSOCIATE DIRECTOR FOR EXTRAMURAL RESEARCH AND TRAINING, NATIONAL INSTITUTES OF HEALTH, ACCOMPANIED BY JOE R. HELD, DVM, DIRECTOR, DIVISION OF RESEARCH SERVICES, NATIONAL INSTITUTES OF HEALTH, AND RICHARD RONK, DEPUTY DIRECTOR, BUREAU OF FOODS, FOOD AND DRUG ADMINISTRATION

Mr. WALGREN. The first witness is Dr. William Raub, who is the Associate Director for Extramural Research and Training at the National Institutes of Health. Dr. Raub is accompanied by Dr. Joe Held, who is Director of the Division of Research Services with the National Institutes of Health, and Richard Ronk, the Deputy Director of the Bureau of Foods for the Food and Drug Administration.

Gentlemen, we are glad you are here and your written statements, if you have any, are to be made part of the record and any written submission you would like to make will be made part of the record, as a matter of course.

So, please, feel free to summarize and cover the ground which you feel should be highlighted in this area.

Dr. Raub.

Dr. RAUB. Thank you very much, Mr. Chairman.

I have some brief oral remarks that are strongly similar to the advanced text that we provided to the committee staff. With your permission I will read it.

I appreciate the opportunity to testify today on behalf of the National Institutes of Health concerning H.R. 6245, the Humane Care and Development of Substitutes for Animals in Research Act.

As Associate Director of NIH for Extramural Research and Training, my area of responsibility includes the policies and procedures governing the more than 20,000 research awards that we make annually. Promoting proper care and use of animals in biomedical research and testing is one of my most important responsibilities.

In appearance before this panel last October, I said,

> It is almost impossible to exaggerate the importance of laboratory animals in the search for new or improved means to prevent, treat and cure human disease. Virtually every major advance in health care stems in whole or in part from research performed with animals.

Such research is essential if we are to continue to make progress toward overcoming such maladies as cancer, heart disease, diabetes, brain dysfunction and environmentally caused disorders.

At the same time, Mr. Chairman, I emphasized that the social imperative that calls for the use of animals in research "is not a license to take animals' lives needlessly, or to inflict pain and suffering that could reasonably be avoided. Abuse of laboratory animals is as inconsistent with good science as it is with good conscience."

I believe that the vast majority of the scientific community and the general public shares that view. It is for that reason, Mr. Chairman, that I can state without qualification today that we are wholly in support of the objectives of the legislation before this committee.

Being of one mind on that point, the question before us is: How can we best work toward insuring proper care and appropriate use

of animals in the thousands of research laboratories throughout the Nation? That there have been lapses in this area in the past, as there are in any human endeavor, cannot be denied. The NIH does not condone that situation, nor does it accept it as inevitable. The challenge is to take a fundamentally sound and generally effective system and make it even better.

The bill under consideration is one approach—an attempt by statute to establish, among other things, a highly specific detailed mechanism under which the use of animals in research and testing would be monitored and governed. It is on this point—on the question of method rather than principle—that we differ. We believe that the authorities now in law and the administrative mechanisms already at hand are adequate if they are utilized fully. What is needed, in our view, is greater emphasis upon refining and strengthening the existing system. We are committed to bringing that about.

A parallel comes to mind here with the system by which human subjects in medical research are protected. That system is based on only a few lines in the Public Health Service Act, specifically section 474. Experience with the protection of human subjects clearly indicates that a broad legislative framework provides an effective base upon which to build a workable system, one with flexibility to accommodate change.

IMPROVED METHODS FOR BIOLOGICAL TESTING

One of the major objectives of the bill is to encourage and promote the development of improved methods for biological testing, especially those that reduce or eliminate the use of laboratory animals. In general, Mr. Chairman, apart from the desire to avoid excessive use of animals, scientists have a very pragmatic reason for seeking and being receptive to such new testing methods. It is easier and faster, all things being equal, to carry out testing on organisms in a laboratory dish than to maintain and work with an animal colony.

The search for improved methods for biological testing is one of the purposes of the national toxicology program [NTP]. Its two-fold mission is to use established methods, including animal testing, to identify chemicals that are toxic, and to develop and evaluate new methods to determine if they can predict human disease as well as, if not better than, established methods.

During 1981, $6.4 million of the national toxicology program budget was devoted to the latter purpose. While the search for improved methods goes on, we must recognize that animal use will be necessary for the foreseeable future. At present we find that in testing chemicals for such properties as carcinogenicity, for example, non-animal-test methods are only 60 to 80 percent as accurate as established animal test methods.

The national toxicology program disseminates information about toxological test results and improved testing methods among its participating Government agencies and to the scientific community at large, so that these methods can be put into practice in a timely and effective manner. In addition, through our regular research project grant system, we identify research results that can lead to

new biological testing methods. As new scientific advances help to unravel the mysteries of toxicity, cancer, mutations, and other biological phenomena, we undoubtedly will be able to develop changes in the methods used to test suspect materials. We are eager to promote and utilize advances that produce reliable scientific results while, simultaneously, reducing our dependence on animals.

Not only would title I of H.R. 6245 duplicate functions of the national toxicology program, this title also would duplicate peer review authorities already in statute or regulation. Moreover we believe the review mechanism prescribed is almost certain to prove unsatisfactory. The prescription leaves out important scientific disciplines and offers far too little flexibility.

ACCREDITATION AND ASSESSMENT

In regard to the accreditation and monitoring of institutions that use animals in research, we believe that present authorities are an adequate base from which to insure that appropriate standards are met. As you know, the primary statute affecting the care and use of laboratory animals is the Animal Welfare Act of 1966, as amended. Responsibility for implementing its provisions and enforcing the regulations derived from it is assigned to the U.S. Department of Agriculture and conducted through the Animal and Plant Health Inspection Service [APHIS]. There is strong support within the biomedical research and animal welfare communities for continuing this arrangement.

The NIH "Guide for the Care and Use of Laboratory Animals" preceded the Animal Welfare Act by 3 years and has been revised and updated periodically since first publication in 1963. Under NIH policy each recipient institution of an NIH award is required to file with our Office for Protection from Research Risks [OPRR] a formally negotiated, written assurance that the institution will follow the guide and comply with all applicable statutes. An acceptable assurance is a prerequisite for an award, and failure to comply with the assurance can result in significant penalties such as termination of an award, recovery of funds previously awarded, or ineligibility for further funding.

We are currently preparing for further revisions in the guide and are developing new policies regarding our review procedures for those projects that use animals. We are also reviewing the structure and function of institutional animal care committees. You have suggested previously, Mr. Chairman, that in addition to veterinarians these committees might appropriately include disinterested individuals, that is, individuals who are not directly associated with the facilities or projects being reviewed. We agree. In this regard it seems of interest to note that of some 650 animal care committees operating in compliance with PHS policy, all but three have doctors of veterinary medicine as members; and of the 650 animal care panels, some 20 percent have nonscientists as members. As the NIH moves to refine its existing guidelines in this area in the coming months, we plan to specify that at least one veterinarian and one nonscientist serve regularly on awardees' animal care committees.

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During my last appearance before this subcommittee, I indicated some changes we then were planning with respect to the initial review process for grant applications involving laboratory animals and our approach to promoting compliance with the awardees' written assurances governing the care and use of laboratory animals.

Our Division of Research Grants [DRG] has issued to members of its study sections some specific directions affecting the documentation of the review of research proposals involving vertebrate animals. Wherever vertebrate animals are to be used, the panel is to address explicitly the appropriateness of the choice of species and the number of animals to be used. It also is to address the justification for the use of animals in terms of the likely results of the research. A judgment is required as to whether the animals will receive proper care and maintenance or whether they are likely to suffer unnecessary discomfort, pain, or injury. Instructions have been issued to executive secretaries within the Division of Research Grants guiding the documentation of these matters in the summary statements, which are the documents of record of the review of grant applications.

Of the approximately 63 review groups in the Division of Research Grants, which comprises a membership of about a thousand leaders in the field of biomedical research, virtually all contain experts in the use of animals and of nonanimal research methodology. Since some two-thirds of our study sections now review applications involving the use of experimental animals, we have taken special care to see that they contain experts in the treatment of animal subjects. In this way we believe that the initial review group remains sensitive to the proper care and use of animals.

As to compliance with the guide, and in keeping with my testimony before this committee last fall, we are developing a system of regular site visits to institutions that conduct research with animals. Among the objectives of the site visits are these: One, to gather data to enable us to make informed decisions on revision of animal care guidelines and their impact on the institution; two, to review institutions that have been cited for deficiencies in the care of research animals. The site visits no doubt will vary somewhat in scope and character from case to case. In general, the representation is expected to include scientists knowledgeable about the kind of research being conducted, a laboratory animal scientist—specifically a veterinarian—an NIH institute representative, and a representative from our Office for the Protection for Research Risks.

In conclusion, Mr. Chairman, I hope it is clear that we endorse the objectives sought by the bill and differ only over the means for reaching them. We believe that current authorities will enble us to do everything reasonable to insure proper treatment of animals used in research and to foster improved methods of biological testing.

Because of the short time we have had to study this specific legislation, my remarks today were necessarily brief and touched on only the major issues.

We would appreciate the opportunity to present to the subcommittee a more detailed statement of our views. I also would be

pleased to respond now as best I can to any questions that you may have, Mr. Chairman.

[The biographical sketch and prepared statement of William Raub follows:]

Department of Health and Human Services

National Institutes of Health

Biographical Sketch

NAME: William F. Raub

POSITION: Associate Director for Extramural Research and Training, Office of the Director, National Institutes of Health

BIRTHPLACE AND DATE: Alden Station, Pennsylvania; November 25, 1939

EDUCATION: A.B., Wilkes College, 1961;
Ph.D., University of Pennsylvania, 1965

1975-1978: Associate Director for Extramural and Collaborative Programs, National Eye Institute
National Institutes of Health

1969-1975: Chief, Biotechnology Resources Branch
Division of Research Resources
National Institutes of Health

1968-1969: Acting Chief, Special Research Resources Branch
Division of Research Resources
National Institutes of Health

1966-1968: Health Scientist Administrator
Special Research Resources Branch
Division of Research Facilities and Resources
National Institutes of Health

1965-1966: Instructor/Post-Doctoral Fellow
Department of Physiology
University of Pennsylvania Medical School
Philadelphia, Pennsylvania

STATEMENT BY

WILLIAM F. RAUB, PH.D.

ASSOCIATE DIRECTOR

FOR

EXTRAMURAL RESEARCH AND TRAINING

NATIONAL INSTITUTES OF HEALTH

Mr. Chairman and Members of the Subcommittee:

I appreciate the opportunity to testify today on behalf of the National Institutes of Health (NIH) concerning the Humane Care and Development of Substitutes for Animals in Research Act. As Associate Director of NIH for Extramural Research and Training, my area of responsibility includes the policies and procedures governing some 20,000 research projects that we fund annually. Promoting proper care and use of animals in biomedical research and testing is one of the most important of my duties.

The Principle of Animal Protection

In an appearance before this panel last October, I said "it is almost impossible to exaggerate the importance of laboratory animals in the search for new or improved means to prevent, treat and cure human disease. . . . Virtually every major advance in health care stems in whole or in part from research performed with animals." Such research is essential if we are to continue to make progress toward overcoming such maladies as cancer, heart disease, diabetes, brain dysfunction and environmentally caused disorders.

At the same time, Mr. Chairman, I emphasized that the social imperative that calls for the use of animals in research "is not a license to take animals' lives needlessly, or to inflict pain and suffering that could reasonably be avoided. Abuse of laboratory animals is as inconsistent with good science as it is with good conscience."

I believe the vast majority of the scientific community and the general public share that view. It is for that reason, Mr. Chairman, that I can state without qualification today that we are wholly in support of the objectives of the legislation before this Committee.

Being of one mind on that point, the question before us is: How can we best work toward ensuring humane care and appropriate use of animals in the thousands of research laboratories throughout the nation? That there have been lapses in this area in the past, as there are in any human endeavor, cannot be denied. The NIH does not condone that situation, nor does it accept it as inevitable. We believe this goal can--and must--be achieved.

The bill under consideration is one approach: an attempt, by statute, to establish, among other things, a highly specific and detailed mechanism under which the use of animals in research and testing would be monitored and governed. It is on this point, on the question of method rather than principle, that we differ. We believe that the authorities now in law and the administrative mechanisms already at hand are adequate if they are utilized fully. What is needed in this area is a further emphasis upon refining and strengthening the system by which we seek to promote compliance with the regulations, standards and principles under which research with laboratory animals is conducted. We are committed to this goal.

A parallel comes to mind here with the system by which human subjects in medical research and practice are protected. That system is

based on only a few lines in the Public Health Service Act, Section 474. Experience with the protection of human subjects clearly indicates that a broad legislative framework provides an effective base upon which to build a workable system, one with flexibility to accommodate change.

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The search for improved methods for biological testing is one of the purposes for which we developed the National Toxicology Program (NTP). Its two-fold mission is: to use established methods, including animal testing, to identify chemicals that are toxic, and to develop and evaluate new methods to determine if they can predict human disease as well as, if not better than, established methods. During 1981, $6.4 million of the NTP budget was devoted to the latter purpose. While the search for improved methods goes on, we must recognize that animal use will be necessary for the foreseeable future. At present, we find that in testing chemicals for such properties as carcinogenity, for example, non-animal test methods are only 60 to 80 percent as accurate as established animal test methods.

The NTP disseminates information about toxicological test results and improved testing methods among its participating Government agencies and to the scientific community at large so that these methods can be put into practice in a timely and effective manner. In addition, through our regular project grant system we identify research results that can lead to new logical testing methods. As new scientific advances help to unravel the mysteries of toxicity, cancer, mutations and other biological phenomena, we undoubtedly will be able to develop changes in the methods used to test suspect materials. We are eager to promote and utilize advances that produce reliable scientific results while, simultaneously, reducing our dependence on animals.

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institution of an NIH award is required to file with our Office for Protection from Research Risks (OPRR) a formally negotiated, written assurance that the institution is committed to following the Guide. An acceptable assurance is a prerequisite for an award, and failure to comply with the assurance can result in significant penalties--termination of an award, recovery of funds previously awarded or ineligibility for further funding.

We are currently preparing further revisions in the Guide and are developing new policies regarding our review procedures for those projects that use animals. We are also reviewing the structure and function of institutional animal care committees. You have suggested previously, Mr. Chairman, that veterinarians and lay persons routinely be members of such bodies. We agree. In this regard, it seems of interest to note that, of some 650 animal care committees operating in compliance with PHS policy, all but four have veterinarians as members; and of the 650 animal care panels, some 20 percent have non-scientists as members. As the NIH moves to refine our existing guidelines in this area in the coming months, we plan to specify that at least one veterinarian and one non-scientist serve regularly on awardees' animal care committees.

During my last appearance before this Subcommittee, I indicated some changes we then were planning with respect to the initial review process for grant applications involving laboratory animals and our approach to promoting compliance with the awardees' written assurances governing the care and use of laboratory animals.

99-706 O—82——3

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As to compliance with the Guide, and in keeping with my testimony before this Subcommittee last fall, we are developing a system of periodic site visits to institutions that conduct research with animals. Among the objectives of the site visits are these: (1) to

gather data to enable us to make informed decisions on revision of animal care guidelines and their impact on the institution and (2) to review institutions that have been cited for difficulties in the care of research animal care. The site visits no doubt will vary somewhat in scope and character from case to case. In general, the representation is expected to include scientists representing the research being conducted, a laboratory animal scientist (veterinarian), an NIH Institute representative and one OPRR representative.

Conclusion

In conclusion, Mr. Chairman, I hope it is clear that we endorse the objectives sought by the bill and differ only over the means for reaching them. We believe that current authorities will enable us to ensure humane treatment of animals used in research and to foster improved methods for biological testing.

Because of the short time we have had to study the legislation, my remarks today were necessarily brief and touched only on the major issues.

I will be pleased to respond to any questions you may have.

Mr. WALGREN. Thank you very much, Dr. Raub. I think it certainly is clear that you are pursuing concerns of the subcommittee with real purpose and I think you and the NIH deserve a great deal of credit for that.

Perhaps I could ask a few questions and then go to the other members——

The bill under consideration specifically requires research entities receiving Federal moneys to have privately accredited animal facilities as well as institutional animal care committees, and they must provide assurances to that effect to the funding agency.

The question is, do you feel that such requirements would be overburdensome to a research entity?

Dr. RAUB. We can't say with certainty now that the requirements definitely would be overburdensome. Our concern is that they might be, and we believe that a more gradual development of our current systems—which encourage the use of private accreditation but offers some more flexible options for those institutions that don't have as complex a set of facilities or requirements—may be more appropriate. One of the questions that we plan to continue exploring will be the best balance among those very high standard accreditation systems and other approaches that can meet various legal and other requirements that perhaps may be substantially less expensive both for the institutions and for the Federal agencies involved.

Mr. WALGREN. I certainly would appreciate it if you would give us some specific ideas on what those other options might be. We would really appreciate knowing what other avenues there might be, in your view, that would serve the same purposes as the requirement for the private accreditation system.

Dr. RAUB. I would be glad to do that, Mr. Chairman.

[The information follows:]

With regard to non-Federal accrediting bodies, we believe that the existing and functioning American Association for Accreditation of Laboratory Animal Care (AAALAC) has demonstrated that it is well qualified to perform the accrediting role. It is a nonprofit organization which utilizes well-trained and experienced personnel dedicated to upholding the standards set forth in the "Guide for the Care and Use of Laboratory Animals." AAALAC not only sets high standards; it also provides recommendations and suggestions to assist animal care facilities to meet those standards.

We do not think it would be appropriate to require AAALAC accreditation for all federally funded research facilities. There are many institutions, especially smaller ones, that cannot afford the costs of AAALAC accreditation. For those institutions the present policy requiring them to provide the Public Health Service with assurances that they are progressing toward full compliance with the standards of the "Guide for the Care and Use of Laboratory Animals" seems more realistic.

Mr. WALGREN. The NIH has encouraged public participation in scientific decisionmaking by including nonscientists in the membership of the Institutional Review Boards for research on human subjects and on DNA advisory committees. Could you discuss your experience with these public members and whether or not they have been valuable to the process and the progress of research in those two areas?

Dr. RAUB. With specific respect to both the human subjects protection procedures and the guidelines related to DNA, our experience not only has been positive, Mr. Chairman, but we believe the perspective provided by the nonscientists has been invaluable. That

also has been true for our National Advisory Councils, which for many years have had in statute a requirement for about one-third of the membership to be nonscientist members.

Mr. WALGREN. You indicated in your testimony that you are encouraging the participation of nonscientists and that now 20 percent of the institutional animal care committees have nonscientists as members. Have you considered whether or not it would be helpful to be sure that those nonscientist members were at least not directly involved in the institution as an interested party?

Dr. RAUB. As I indicated in my testimony, Mr. Chairman, we agree completely with the principle that you enunciated previously, of having some disinterested individuals involved in these proceedings. Among the detailed options we have been exploring have been just how to describe that in a way that offers reasonable flexibility for the awarding institutions and yet captures the essence of that principle. So long as we can make clear that the perspective that's needed is from individuals who are not directly responsible or otherwise associated with the research being conducted, we believe that we can go a long way to achieving the kind of involvement and balanced viewpoints that this subcommittee and others have encouraged.

Mr. WALGREN. Could I ask if you could give us in writing some of your specific thoughts in that area. We would appreciate any suggested approaches that you think would be helpful from an agency standpoint, not necessarily for legislation. We are very interested in what you would feel proper from NIH's standpoint to ask of an institution applying for a grant, and any thoughts on how you pursue that association of a noninterested member that the agency has had.

Dr. RAUB. I would be pleased to do that. As a followup to our previous discussions, we have had a staff group working on some of these options and had planned for this summer as a target date to have some specific proposals that we then might begin circulating for discussion within our component institutes and with the institutional community with which we deal. I would be glad to share some of that information in a preliminary form with the subcommittee, Mr. Chairman.

[The information follows:]

We believe that it would be reasonable to include at least one nonscientist on institutional animal care committees. Such individuals would add important perspective to committee deliberations. The choice of the nonscientist representative(s) should be the responsibility of the awardee institution so that the many different perspectives present in the local nonscientific community are most effectively incorporated.

Mr. WALGREN. In your testimony you indicated that one of your reservations about the bill is that it provided a highly specific and detailed process for monitoring and governing research. One of the things we are all trying to grapple with is that certainly in the individual instance that provided some news coverage in this area last fall, there was very little monitoring. Part of our attempt is to provide a detailed monitoring system. At the same time we don't want to be overburdensome.

You indicate that the Department of Agriculture and APHIS in your opinion are still the proper monitoring agencies to rely on.

Perhaps that's putting words in your mouth, but do you feel that monitoring itself is overly burdensome? If we could split out the monitoring versus the governing of the research, do you feel that the monitoring provided by this bill would be inhibitive of things that we all want to happen?

Dr. RAUB. I don't believe the monitoring would necessarily be overly burdensome. I think the main thrust of our concern is that we believe that ample statutory and regulatory authority exists and that, in general, oversight such as the comments and critique that this subcommittee and the sister Subcommittee on Investigations and Oversight have provided do much to insure that a broader perspective is brought to bear on how we interpret and implement our current authorities.

Second, the Animal Welfare Act is quite clear as to the fundamental requirements for facilities and care. We believe that the existing system based in the USDA is fundamentally sound in attempting to insure that the statute meets with appropriate compliance. We would put our efforts into working with the USDA and supplementing that with the new site visits I mentioned and more stylized interactions with the institutions than we have done in the past. We believe that can be more efficient and more effective than any prescriptive legislation.

Mr. WALGREN. Personally, with respect to monitoring, I am skeptical about whether we can get the needed breadth of effort out of the Agriculture Department, and particularly from this administration. The laboratory inspection area is at present, as I am sure it has been in past times and will be at least for a period of time, a kind of orphan sister, or an effort without money. One goal of our bill is to create in the institutional animal studies committee a self-monitoring system, not necessarily costly or invasive. It would put a fiduciary responsibility in a noninterested party, a real public responsibility that most citizens would try to live up to. And it could legitimately be expected that a warning flag would be raised when something was really wrong, rather than having to rely on actual invasive, or onsite inspections of such a frequent nature, to insure that nothing is going wrong.

I would be interested in any thoughts you might have as to whether there is any other avenue that is less invasive, less burdensome, and that would assure us that something really wrong would at least be called to the attention of the authorities in the Agriculture Department rather than their having to ferret it out.

I guess I would be interested in any other thoughts that you might have in that particular area.

Dr. RAUB. Your point is well taken, and we would be glad to respond to that.

Mr. WALGREN. I would like to recognize my other colleagues for their interests, and then I have a couple of other thoughts. Mr. Weber.

Mr. WEBER. Thank you, Mr. Chairman.

Dr. Raub, I have a few different questions. First of all, title I of the act requires that the National Institutes of Health, among other agencies, fulfill a variety of responsibilities in terms of developing new evaluation testing methods. Of particular concern is the promotion of nonanimal test methods.

I want to get some idea from you of the cost included in financing these developing techniques. I presume that such endeavors require some disbursement. Can you give my any kind of an estimate?

Dr. RAUB. Perhaps the best way I can respond to that is to describe the effort already in place that, in large measure, would have at least some of its functions duplicated by title I as written. The national toxicology program is an organized effort based in our National Institute of Environmental Health Sciences, but also involving our National Cancer Institute as well as the Food and Drug Administration, the National Institute of Occupational Safety and Health, and other liaison arrangements with the Environmental Protection Agency and the Consumer Products Safety Commission.

That activity involves both: First, the testing of chemical substances in the environment that may be toxic, especially those that may cause cancer and mutations, and second, the search for new testing methods. That effort currently requires slightly in excess of $60 million per year, about 10 percent of which is currently spent on test methods development.

Mr. WEBER. So, stated simply, we are currently spending about $6 million a year to develop new testing methods?

Dr. RAUB. That is a very conservative estimate only within the national toxicology program. Within the rest of NIH's institutes, there are new and improved methods for testing emerging largely as a byproduct of basic and applied research on biological phenomenon. That is, in the main, the funding of those other institutes is primarily in search of new knowledge about biological systems and their medical applications. As those new insights come about, it is frequently the case that new knowledge can be built upon for some specific new testing method. I don't have good figures as to the extent of that, but it is substantially in excess of the $6 million that is specifically earmarked for test method development.

The long-term plan for the national toxicology program is to shift systematically the proportion of moneys, with a larger and larger fraction going into test method development. There is a large backlog of substances under test in conventional methods that must be completed. In addition, when the program started, there were few other entities in the position to carry out this testing. As the Toxic Substances Control Act is implemented and more and more of the burden of actual testing falls on commercial manufacturers, it will be possible for the Government gradually to circumscribe its actual testing efforts even further, and put more and more of its resources into test method development that will be to the benefit of everyone involved in testing.

Mr. WEBER. So there is a plan currently in place that is actually expanding the Government's investment already in new testing methods. Are some of those funds specifically directed toward development nonanimal means of testing?

Dr. RAUB. Yes.

Mr. WEBER. How extensive are those efforts?

Dr. RAUB. Much of the $6 million that I make reference to in the testimony involves nonanimal systems. By that I mean specifically bacterial cultures that can be used to assess possible genetic damage from chemicals. A biologist will correct me and point out

that a fruit fly is technically an animal, but, for purposes of these discussions, many of these testing methods are also being explored in very simple invertebrate systems such as the fruit flies.

Mr. WEBER. Well, since the bill calls for further action of this type, what new frontiers do you envision exploring before this legislation became law?

Dr. RAUB. In addition to exploring a variety of other systems such as cultured human cells, for example, that can be dealt with analogous to bacterial cultures in laboratory dishes, the long term plan of the national toxicology program calls for looking at other measures of toxicity besides genetic damage and possible causation of cancer. Toxic effects manifest themselves in other organ systems as well as the lung, the kidney, and the liver. And over the long-term there will be need for strong testing methods in these areas for assessing toxicity as well as the current pressing issues for measuring possible genetic damage.

In these other more complicated areas of physiology, it is less obvious that there will be nonanimal systems in the strict definition of that word, that will suffice. But it should be possible in various kinds of isolated organ systems to develop those test methods as far as is scientifically possible to reduce the burden on whole animal testing. And that is indeed the long term goal of this national toxicology program.

Mr. WEBER. I see. Moving on to another point, under title II, the question of accreditation is something that you have addressed before. We talked a little bit about the problems that may be faced by universities during your testimony last fall. I would like to have your comments on how the need to have an outside agency accredit universities could affect those same universities? Also, what percentage of the universities are not in compliance with accreditation standards? Finally, what kind of standards can we expect to see imposed by outside research entities performing the accreditation? Do you have any comments along those lines?

In other words, what kind of burden is this accreditation process going to be on the universities?

Dr. RAUB. It has been estimated that if there were an immediate requirement that certification by AAALAC be a condition of our awards, and that of other Government agencies, that the total cost might be in the range of $500 million——

Mr. WEBER. $500 million?

Dr. RAUB. In one-time investments in facilities to come up to the standard that AAALAC uses.

Now, I hasten to add that the standard that AAALAC uses is deliberately much higher than what is required in the Animal Welfare Act, but it is viewed as generally a high quality environment and set of practices. The NIH policy has been to encourage AAALAC accreditation where an institution has the means and the will to seek it. And we have accepted AAALAC accreditation as virtually prima facie evidence that an institution has adequate facilities. We have not required it as a condition of our awards and have allowed the option of a local committee to operate as well.

Mr. WEBER. One-half a billion dollars is a lot of money—especially when most facilities are somewhat starved for funds these days.

At least, that is the picture we are presented with day after day in this subcommittee.

Can you specify more clearly where those funds will be needed or at least give some idea of where that big chunk of money will be spent?

Dr. RAUB. I can't do it off the top of my head, but I would be glad to provide it to you as a statement.

Mr. WEBER. I would be very interested in that.

[The information follows:]

This provides further information on the cost to NIH grantee institutions to upgrade their laboratory animal facilities to comply with the NIH "Guide for the Care and Use of Laboratory Animals." That cost has been estimated to be $500 million. This estimate is based on information contained in the "National Survey of Laboratory Animal facilities and Resources," completed by the National Academy of Sciences in 1978.

An overview of the survey is contained in the executive summary on pages 5 through 11 (the Executive Summary is printed below). At the top of page 10, the authors state that the survey estimated a requirement of "350 million . . . to meet current needs of nonprofit biomedical research organizations for space replacement, remodeling, and additions." In 1982 estimates, the construction costs of 1978 need to be increased by about 40 percent; thus, the $350 million becomes $500 million. The survey also estimated that "another $407 million . . . will be required to meet space needs projected for fiscal year 1988." We have not considered any new space requirements or projected needs in any of our plans or estimates for replacement or remodeling, so the $500 million is likely to be a minimal estimate for future years.

The staff of the NIH Animal Resources Program, Division of Research Resources, has also studied this question in some detail and has talked to many grantee institutions. We have over 600 grantee institutions using animals. Many need to totally replace their animal facilities. None estimate their cost for this at less than $5 million and some will require more than $10 million. Those in need of renovation, especially renovations involving heavy fixed equipment (e.g., air conditioning or cage washing), estimate their cost at $700,000 to $1.2 million per facility. While we are reluctant to extrapolate a total national need from these informal findings, they are empirical evidence that the $500 million figure is very conservative.

EXECUTIVE SUMMARY

This is a report of a national survey of laboratory animal facilities and resources conducted by the National Academy of Sciences, National Research Council Institute of Laboratory Animal Resources, at the request of the Animal Resources Program Branch of the NIH Division of Research Resources. Two earlier surveys (reported in 1964 and 1970) had been conducted by ILAR at the request of NIH. Since these reports were published, many changes have taken place and, therefore, much of the information in the first two surveys is no longer relevant. It was deemed essential that updated information be developed.

The third survey was aimed at the collection and analysis of objective data on the current status of unfilled needs in, and future requirements for research animals, animal resource personnel, facilities and programs throughout the United States during fiscal year 1978. Although primary attention in this report is given to nonprofit organizations that were eligible for Federal grants and that conducted biomedical research during fiscal year 1978, data were also received from Federal agencies, commercial research laboratories, the pharmaceutical industry, and nonprofit organizations that used animals for purposes other than biomedical research.

Appropriate data processing techniques were used to enter the data in the NAS-NRC computer; and the accuracy of data-processing procedures and the validity and consistency of data provided by respondents were ensured by continuous editing.

Survey questionnaires were distributed to 2,637 known users of laboratory animals in the United States, and 1,902 (72 percent) were returned. Of these, the responses of 1,252 organizations (47 percent of those solicited) fulfilled the criteria of the authoring committee (ILAR Committee on Laboratory Animal Facilities and Resources) [1] for inclusion in the response population for aggregate analysis. These or-

[1] Membership of Committee: C. Max Lang. (chairman), John G. Adams, Emerson L. Besch, Richard R. Fox, Robert R. Jorgensen, William A. Knapp, Jr., James R. Pick, Jr., Stefano Vivona, Samuel Abramson (staff officer).

ganizations included 992 nonprofit, NIH-grant-eligible institutions (including 489 biomedical research organizations with annual research budgets of at least $5,000), 137 commercial institutions (including 52 member firms of the Pharmaceutical Manufacturers Association), 25 components of the Department of Defense (DOD), 21 units of the U.S. Department of Health, Education, and Welfare (DHEW), and 77 components of other Federal agencies. The biomedical research organizations included 69 schools of medicine, 10 schools of veterinary medicine, 42 other health professional schools (dental, public health, life sciences, etc.), 149 universities and colleges, 76 universities with affiliated professional schools, 65 hospitals, and 78 Federal-grant-eligible research institutes or laboratories.

Separate sections of the report are devoted to the following topics: dimensions of survey populations, animal use and sources, facility administration and personnel, facilities and equipment, costs of animal care, and appendix (the survey questionnaire). Each of these sections has two parts: current status, and comments and projections. In selected areas of interest, comparisons are made between the data derived from the fiscal year 1968 and fiscal year 1978 surveys.

Major Findings and Conclusions

ANIMAL USE AND SOURCES

The number of laboratory animals acquired during the last decade (between the fiscal year 1968 and fiscal year 1978 surveys) has decreased. Nonprofit biomedical research organizations reported decreases in the acquisition of mice, carnivores, sheep and goats, birds, and nonhuman primates. But when the data were summarized for all respondents, there was a decrease in acquisitions of all species except other rodents, swine, and cattle and horses. These changes during the past 10 years could have resulted from any of the following factors: noncomparability of survey respondents, substantial reduction in breeding colonies maintained for in-house production, and decreases in available funding, available space, and/or ability to comply with current guidelines for housing and care.

The majority of respondents that acquire animals from their own breeding sources do not maintain genetic records. This is regarded by the committee as a substandard practice that is incompatible with quality research.

The changes during the last decade in the total number and species of animals used may have been affected by the substantial changes in the research methods during this period. For example, shifts from short-term animal studies to longer-term studies, increased awareness of environmental factors that may affect research data, and increases in the kinds of investigation that require containment housing would all tend to reduce the efficiency of space use.

The substantial decrease in the number of nonhuman primates is almost certainly because of their reduced availability and increased cost. The substantial increases in average daily inventory and length of stay suggest that those now available are being conserved for essential long-term studies or breeding colonies.

The committee believes that the overall decrease in acquisition of animals from own breeding sources is due to several factors: lack of animal space, unit cost per animal is higher than for those commercially available, greater variety available from commercial sources, requirement for uniformity in animals to obtain reproducible results, and ready availability to investigators.

The committee believes that in the next decade, scientists will rely increasingly on commercial sources for acquisition of animals that are known to be of good quality and defined genetic background.

The number of nonprofit biomedical research organizations importing animals from outside the continental United States (7 percent) is of concern to the committee because of the possibility of introduction of diseases that are not indigenous to this country or for which there is no effective means of diagnosis or control. Precautions should be taken in establishing quarantine, in-house testing, and methods of introducing animals and biologic material into a research facility to prevent serious epidemics of disease.

Facility administration and personnel

Approximately 82 percent of all responding organizations stated that they were in compliance with DHEW guidelines for care and use of laboratory animals. A substantial number of these organizations stated that this compliance was determined by their own institutional committee, or on the basis of such miscellaneous standards as "certification by department chairman," "exercise of local supervision," or "state inspection." This could reflect a high level of institutional concern for humane animal care or a lack of familiarity with DHEW guidelines.

During the last decade there has been a surprisingly small increase in the number of nonprofit organizations that achieved peer recognition of compliance with DHEW guidelines for care and use of laboratory animals, i.e., accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC). For unknown reasons, the relatively high number of organizations (over 370) planning to apply for accreditation at the time of the fiscal year 1968 survey did not, or could not, achieve that status by fiscal year 1978.

Personnel changes during the last decade reflect, primarily, an emphasis on quality animal care—i.e., an increase in veterinarians trained in laboratory animal medicine. This trend is expected to continue at least through the next decade.

Facilities and equipment

Nonprofit biomedical research organizations reported having a total of approximately 10 million net square feet (nsf) of laboratory animal facility in use or under construction in fiscal year 1978, an increase of approximately 2.5 million nsf over the space reported in the fiscal year 1968 survey. The estimated replacement value of this space is $1.4 billion.

Animal facility space use is devoted primarily to biomedical research activities; the median was approximately 70 percent. This is similar to that reported in fiscal year 1968.

Approximately 16 percent of all nonprofit biomedical research organizations reported a need for replacement of some animal facility space now in use, 38 percent reported a need for remodeling to protect the integrity of space now in use, and 43 percent reported a current need for additional space.

Approximately $350 million is required to meet current needs of nonprofit biomedical research organizations for space replacement, remodeling, and additions. Another $407 million (using fiscal year 1978 estimated construction costs) will be required to meet space needs projected for fiscal year 1988.

Nonprofit biomedical research organizations reported a current need of $43 million for equipment renovation, replacement, or additions.

It is surmised that the failure to acquire space and equipment may have been a factor in some organizations' reports of inability to comply with DHEW guidelines for animal care. If that is true, it emphasizes the crucial need for funding to support the replacement, remodeling, construction, and equipping of laboratory animal facility space.

The committee believes that biohazard containment space and equipment needs reflect changes in research activities, as well as an awareness in the biomedical research community of the need to contain hazardous agents. It is recognized that not all organizations are engaged in research with hazardous agents, but the substantial needs reported suggest that there should be priority funding for fulfilling these needs.

The increase in the availability of diagnostic laboratory equipment, plus the current needs, reflect an awareness of the importance of diagnostic laboratory support as an aid in providing high-quality animal care and increasing the reliability of research data especially in long-term studies.

Costs of animal care

Nonprofit biomedical research organizations reported expenditures of approximately $2.2 billion for biomedical research in fiscal year 1978. This represents a substantial increase (28 percent), when corrected for inflation, over expenditures reported in fiscal year 1968. Approximately $800 million (a 1 percent increase over adjusted fiscal year 1968) of this amount was for research projects involving the use of some laboratory animals, of which $571 million (a 7 percent increase over adjusted fiscal year 1968) was furnished by grants and contracts from the NIH.

Approximately 35 percent of the total biomedical research budget is for research projects involving the use of laboratory animals, an apparent decrease from the 44 percent reported in fiscal year 1968; the decrease suggests that other aspects of research are increasing in cost at a slightly greater rate than animal care.

In spite of the increase in biomedical research funds, recovery of animal care costs has not kept pace with actual costs. User fees, including per diem costs, vary widely and do not appear to have achieved the level of cost-accounting that is necessary to ensure an equitable distribution of costs on a direct-charge basis.

Although the user fee, including the per diem charge, is only one of many possible mechanisms of apportioning direct costs to research projects, it can—if properly determined— be the most accurate basis for assessing equitable costs.

Financial accountability of animal care programs can be expected to receive increasing attention in the next decade. Primary factors that can help to achieve effi-

ciency include centralization of animal care programs within the research organization and the use of cost-accounting [2] as a more effectve management tool.

Mr. WEBER. I have one last area of questioning that is of special interest to my district.

I presume that this legislation, if it were enacted, would have some impact on universities that engage in testing on agricultural animals, livestock. I am not referring to standards that might be imposed on packing houses or feeder lots or anything like that, but on testing that is performed on cattle, hogs, and sheep in major university facilities. Is that your understanding of the legislation and do you have any comments on the nature of that impact?

Dr. RAUB. My understanding is that it would impact, as the statute is drafted. However, I am not positive of that. It might depend on the interpretation that one places on the words. I have no firsthand way to gauge what the impact of that would be beyond the general impacts on research. The specific concerns that we had raised had more to do with the regulatory and administrative burden on the institutions themselves in overseeing the research underway. And if the bill applies to the research that you indicate, then it seems to me the same burden carries over.

Mr. WEBER. I see. I have no further questions, Mr. Chairman. Thank you, Doctor.

Mr. WALGREN. Thank you, Mr. Weber. Mr. Shamansky.

Mr. SHAMANSKY. Good to see you again, Dr. Raub. I apologize for being late, but I do want to assure you that while I came in during the middle of your testimony, I have read the part that I didn't listen to.

It seems to me, basically your testimony is a defense of the status quo ante in all substantive fashions. Nothing substantive has changed, it seems to me, since our last get-together here. You really don't want any changes at all and the problem in my opinion is that you don't see institutional problems the way it is now set up.

For instance, on page 5 of your testimony, you say in the first full paragraph, "We are also reviewing the structure and function of institutional animal care committees." After this many months, the idea that you are still studying this chills me a little bit. The testimony brought out last fall that you are letting people investigate themselves. And that is a conflict. You have to take my word for it as a lawyer, that sets up a conflict. The issue is not do we have nonscientific members on the committee—you have got 20 percent of those already—the problem is that the members of the animal care committee are employed by the outfit that is being investigated. No awareness in your testimony that this is an institutional problem; a conflict of interest, where the vets or the nonvets, whoever it is, have a reason to say this is OK. There is no independent member on those animal care committees who is independent in the sense that his livelihood does not depend on the institution. There is just no awareness of the problem here in your testimony. And I can assure you being trained in the law, that is a real problem in this institutional setup, in my opinion.

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[2] "Cost Analysis and Rate Setting Manual for Animal Resource Facilities." Rev. October 1979. NIH Publication No. 80-2006.

Your choice of words is always extremely careful and I greatly respect your use of the English language but if you turn in your testimony to pages 6 and 7, beginning at the very bottom of page 6 and go to the top of page 7, I am intrigued at the use of the words "to gather data", and then, "to review institutions." I really don't know what you mean by "to review". I don't know what a review is. You certainly carefully chose not to use the word inspect at any point in this process. There is no thought here of inspecting something. Maybe that was never the intention. Maybe the law presently doesn't require an inspection. What we learned last time was that there wasn't an inspection. Basically, your testimony on page 6 shows that once again we are dealing in paper. We are handling papers. As long as the file has the requisite papers, the review is OK. It can be done at an office in Washington or wherever, but the institution will not be defiled by someone coming in and actually looking at the conditions.

Now, Ohio State University is in my community and they are concerned—they had the AAALAC inspection and the most important laboratories do. You rejected the idea of monitoring and not by the Government. I feel that is very unfortunate. I think, to me at least, it shows a significant refusal or lack of awareness or lack of sensitivity as to what the problem is.

Nothing has changed basically except better intentions. You are going to do it better and it has taken 6 months and you are still thinking about the content of what these care committees might be.

Still missing the fact—you say you plan to specify at least one nonveterinarian and one nonscientist. But still not independence, which is the key as far as I am concerned.

I don't know how you would find out about a failure to comply, except happenstance. You are not going to send anyone in to inspect and the problem is that the current method of inspection is dependent upon Federal money, and there is going to be less of it, and there will be fewer inspectors. There is no reason to believe that you are going to get more inspectors available to you to inspect what you are charged with than any of the other inspection arms of the Federal Government unrelated to this. They are all going by the boards. And you must be aware of that. I can't believe that you are not.

Your statement is that there is ample statutory authority—yes, there is, institutionally. But, it can't buck the institutional interest that you have, and the money restraints that you are—I am not suggesting that money restraints are your fault, but they are real and you have to operate under them.

And there are real consequences that flow from that. So, as you know, you and I have gone over this before. I am very much interested, and I think animal research is vital. I am not challenging that, and I think this legislation fairly and objectively attempts to meet the problems of both the laboratories' and the public's interest. Having unburdened myself with this concern, I would invite a response.

Dr. RAUB. I appreciate the chance. Mr. Shamansky, I don't think we either misunderstand or fail to appreciate the point you have made, and I think your critique is valid.

I don't regard my testimony or my oral statement as simply a defense of the status quo ante. The thrust of the testimony is that we differ about the need for additional legislation, especially highly prescriptive legislation. We believe that we can build on the existing legislative and regulatory framework to improve the system in the directions that you have raised.

The constraints of funds are significant. Equally important as the constraint of funds is the strong message from the citizens of this country that, in general, they want to see less government than more. And as we move to design and implement this pattern of regular visits on the part of NIH, not only for cause, but also on a random basis to help satisfy ourselves that those statements of assurances are real—to look behind what you aptly characterized as the "paper fortress" in our earlier discussions—we intend to do this in a way that not only builds on the strong positive relationship between NIH and those awardee institutions but also fits both the constraints on dollars and the desire for regulatory simplification. We believe we can achieve those goals. Much of the time since we last discussed this with you formally has been spent in building a consensus within the Federal agencies and with the awardee community that some departure in this direction is indicated.

Mr. SHAMANSKY. But there is no departure that I can discern, no departure in your testimony.

Dr. RAUB. Specifically, when we testified last, we indicated two things that we were going to set about doing. One was improving the quality of the documentation with respect to the care and use of animals——

Mr. SHAMANSKY. I always want better documentation. The beauty is in the eye of the beholder there. It is still a paper chase.

Dr. RAUB. But we also said we would develop this system of site visits. The plans for that are well along, and we expect to have a specific set of proposals available this summer.

Mr. SHAMANSKY. But again your choice of words are very careful to review institutions. What does that mean?

Dr. RAUB. We have deliberately avoided the use of the word inspection. That's true.

Mr. SHAMANSKY. I understand that. And I want to know what you think review means in this context. When the problem is inspection.

Dr. RAUB. We are not convinced that the problem is inspection.

Mr. SHAMANSKY. OK. At least we have got that on the table. The problem is not inspection in these cases.

Dr. RAUB. Well. I believe at the moment at least, we need better understanding of the nature and the extent of the compliance with these statements of assurance, but we also need to understand the constraints under which the institutions operate, and the varied interpretations to which our guide and other guidelines are made.

Mr. SHAMANSKY. There is nothing in your testimony that would indicate that the National Institutes of Health, your division, is still aware of the problem of conflict of interest. You haven't addressed that at all.

Dr. RAUB. I understand your point.

Mr. SHAMANSKY. That is a fatal deficiency.

Thank you, Dr. Raub. Mr. Skeen.

Mr. SKEEN. Thank you, Mr. Chairman.

I see the phrases, "limit animal pain and distress," "minimize animal pain and distress," used repeatedly in this bill.

Can either of the panelists define this language in universally understood terms? If we are going to make informed and responsible judgments, we must be able to quantify important concepts such as distress.

Dr. HELD. Mr. Skeen, you have touched on an area that is a very difficult one to deal with in an objective manner. There is no really good objective measurement for pain or distress, in any species. There have been a number of symposia recently on this subject which have received a great deal of attention from both the biomedical research community as well as philosophical community. I think it is fair to say that nobody has really come up with a good measure of pain and distress.

The issue is one that you just have to trust to professional judgment under particular circumstances and this is something that NIH guidelines attempt to do. For example, over the years we have been concerned with alleviating pain, by providing analgesics or anesthesia to prevent pain. I think that most of us who work in research facilities, those of us who are trained as doctors of veterinary medicine and those trained in medical sciences of various kinds, can have a pretty good idea of when an animal is undergoing a painful experience and can take measures to prevent that. But it is a very difficult thing to legislate and I don't know of any place in the world where this has been done effectively.

Mr. SKEEN. Unfortunately, this creates a dilemma in the bill's implementation. Loose language can be interpreted in many conflicting ways. On whose judgment are you to rely? Is there a way or is there a measurement of stress? Can stress be scientifically measured? Are there limits?

Dr. HELD. Well, there are some ways of measuring stress. In experimental situations this is done by those who do certain types of behavioral research, for example. And certainly in certain types of toxicology testing it is done. However, when you look at the broad regulation of animal care in general, there is no effective way of measuring stress in practical, everyday situations.

Mr. SKEEN. So, the criteria is going to be primarily judgmental then.

Dr. HELD. That's correct, sir.

Mr. SKEEN. Thank you very much. Thank you, Mr. Chairman.

Mr. WALGREN. Thank you, Mr. Skeen.

My understanding is that we are not trying to legislate limits on pain, but to require a judgment about what is appropriate or reasonable by people who presently are in a position to make such a judgment. We want to be assured that those who are responsible for funding this effort and making these judgments focus on that question. Is that your interpretation of where we are going with this legislation, Dr. Raub?

Dr. RAUB. That was my interpretation of the objective of it, yes.

Mr. WALGREN. I want to go back to the $6.4 million that the national toxicology program is spending in the nonanimal testing area. I understand that there is an effort once a test under the budget of the national toxicology program has been developed, to

transfer this function to the private sector. Can anyone tell me how complete that transfer has been? In other words, in that $6.4 million that we are presently spending on testing, how long have those tests been developed and to what degree has there been a transfer out of the the national toxicology program and into the private sector for implementation of previously developed tests.

Dr. RAUB. I would be glad to provide a statement to that effect. [The information follows:]

Over the past decade, much research has been carried out with the goal of developing quicker and less expensive methods for determining the toxicity of chemical compounds. This research was stimulated by developments in the field of mutagenesis, as well as by discovery that in a number of instances evidence of mutagenicity can be evidence that a compound is carcinogenic. In addition, there has been increased awareness of the extent to which we live in a world filled with a wide variety of chemical compounds (both natural and synthetic) about which little is known.

The need to learn more about the extent to which these chemicals pose a hazard has stimulated major research efforts. The sheer number of these chemicals, increasing each year, has caused the scientific community to look for faster and less expensive methods of toxicity testing than have been available in the past. Over the past three and one-half years the National Toxicology Program (NTP) has been at the forefront of that effort.

While major advances have been made in this area, it is not likely that non-animal tests will ever totally supplant the use of animals in toxicity testing. What is to be hoped is that over time the use of animal testing will be confined to those specific cases where non-animal test methods will not suffice and that this will be accompanied by a reduction in the numbers of animals used in toxicity testing. There is considerable discussion among scientists about the new technology; however, it is still too early to say that any of these tests can completely supplant the use of test methods utilizing animals. There are continuing efforts to evaluate these tests. For example, NIH sponsored the development of the recently completed International Program to Evaluate Short-Term Tests for Carcinogenicity.

This program, begun in 1977, included some 65 scientists from 12 countries. Its main objective was to compare the relative efficacy of 30 especially promising short-term tests for mutagenicity and carcinogenicity. The test systems that were used in this international collaborative study ranged from phage and bacteria, fungi, and mammalian cells in culture to whole-animal systems. The results of this study will be helpful in long-term efforts to develop alternatives to the use of animals in at least certain aspects of toxicology testing.

The following paragraphs describe particular activities of the NTP focused on test method development and improvement.

Non-human mammalian species are appropriate surrogates for humans in efforts to determine the toxic potential of chemicals because of biological similarities involving complex interactions of various organ systems such as the cardiovascular and the central nervous system. These interactions cannot be duplicated in in vitro systems. A major objective in developing test methods is enhanced predictive value from both scientific and resource standpoints. To this end, selected in vitro or in vivo systems are being developed or utilized that permit wiser choices regarding which chemicals require more extensive animal studies. An in vitro system or an in vivo system that uses fewer animals to indicate that additional extensive animal tests are not warranted, or are of low priority, represents better science and reduces the number of animals used in testing.

The NTP has implemented a testing rationale which requires the execution and evaluation of certain test results prior to making a decision to carry out a two-year animal study that invovles 600 rats or mice. In one such test, 30–40 rats are used to determine the biological fate of a chemical; i.e., how it is absorbed, where it goes in the body, how long it is retained and in what form, and how it is excreted. Such tests can result in a more effective use of animal species. If traditional procedures were followed, a two-year study would have been conducted wherein animals would have been exposed by oral route to an NTP priority chemical (in this case, hexachlorocyclopentadiene). The newer studies on biological fate clearly demonstrate that the oral route of exposure would have yielded a meaningless study result and would therefore have been a wasteful use of 600 animals.

A further example of better use of test methods involving limited numbers of animals is the benzidine initiative. Interim results from these studies show that essentially all chemicals in this class are converted in the body to a chemical that is a

known carcinogen. Thus, once the data on a representative sample of this class establishes the scientific validity of the principle, it will not be necessary to conduct experiments on every chemical in this class using 600–800 animals.

Another series of tests is being used to aid in setting priorities for extensive two-year animal bioassays. In this effort, five or six in vitro tests are done to determine whether a chemical can cause genetic damage, i.e., point mutation, chromosome change, unscheduled DNA synthesis, or cellular transformation. Again, the utility of these tests is to permit more effective selection of chemicals that warrant extensive animal studies. While these testing procedures were not designed to supplant animal tests altogether, if they did not exist animals would be used in this phase of testing. It is possible that once more extensive validation has occurred, some of these tests may selectively replace animal tests. It will take at least another decade of research to develop the tests to that point. However, it is likely that it will always be necessary to use animals for some types of toxicity testing.

Mr. WALGREN. If I could ask Dr. Ronk about the interaction between the toxicology program and the FDA, and how would the FDA use the data that the toxicology program might develop concerning nonanimal methodologies for food and drug toxicity testing?

Dr. RONK. Thank you, Mr. Chairman. FDA interacts with the national toxicology program in a number of ways, either through the National Center for Toxicological Research in Arkansas, or through the bureaus either here at headquarters or in field locations. We serve on many of their committees, we serve on—I think the Commissioner of Food and Drug is presently the program chairman for the national toxicology program, so there is much forward planning about what types of tests will be done and how they implement many of them—or complimentary to much of the research that is carried out by the Food and Drug Administration. Many of the short term tests that are presently nearing state of the art kinds of considerations so that they can be used for regulatory purposes, are the type of tests that were described, short term tests which could be used instead of long term chronic studies for prediction of whether or not a material has a potential to cause cancer. These tests are presently used by FDA for screening compounds and they are clearly used by much of the industrial component to do that type of job. We don't believe, however, that they can resolve the issue yet, about whether or not something is a carcinogen in human beings, but we think that they are able to point the way in some regards. We are also interested in substitute tests that we might use in the cosmetic area. We are especially interested in tests that might be used to substitute for the Draize test, used to test the effects of cosmetic products on the eye area. So we are very aware of what is going on in the national toxicology program and we have an ability to influence the type of testing that they do undertake.

Mr. WALGREN. I see. Dr. Raub, you indicated that title I, which is this area of nonanimal testing, in your view, left out some scientific diciplines and was relatively inflexible. Could you develop that?

Dr. RAUB. Yes, Mr. Chairman. Just as a few examples, there are some critical areas related to microbiology and cell biology that are not explicit in the list of scientific disciplines, and yet would be critical to the development of the kinds of testing and the review of the kinds of applications that are suggested here.

The intent was mainly not to find fault with the areas of science and technology that were made explicit, but rather to point out

that there are other disciplines that had gone unmentioned—to illustrate the complexity of the problem.

With respect to the flexibility under the statutes and regulations we now have governing us, we have the authorities to establish both standing committees and ad hoc groups. As a general rule, when we have a large volume of application traffic of a relatively homogeneous sort in a particular area, it seems worthwhile in terms of management and cost to make a standing committee. Whereas, when we have a relatively small number of applications in a certain area, or special problems as inevitably happens at the frontiers of research, a standing committee isn't quite properly configured and so we establish an ad hoc group. Our concern therefore is that any body established in law might quickly be overtaken by the developments in science and by the flow of applications and while clearly not intended by the bill, the result could be a distinctly suboptimal peer review, because of the apparently inflexibility in it. By contrast, the current system, which allows us to make a judgment and bring together either an ad hoc group or enrich an established group with ad hoc consultants, gives us the breadth and depth of expertise that we need.

Mr. WALGREN. The bill provides for an advisory committee as opposed to a standing or an ad hoc group. There is a design to focus the attention of the establishment in NIH on this area. I guess I don't understand how that advisory panel would restrict your ability to move ad hoc and standing groups to the areas where you feel they would be most helpful.

Dr. RAUB. Perhaps we had interpreted something other than the intent of the legislation, Mr. Chairman. I recall that, in the discussion draft that was circulated last January, there was a specific reference to an ad hoc study section. The bill as introduced last week, as you point out, refers to a special advisory panel. In the context that it is written and using as it does words like "review" which has a precise statutory meaning in terms of our peer review system, we interpreted the bill to require a peer review event on the part of that committee. I also see how the language can be read to mean some advisory group that would sit astride the regular peer review process and make more general kinds of observations and critique. One of the things we had planned to speak to in our more detailed statement for the subcommittee would be the several interpretations we had placed on title I and offer our perspective on those alternatives.

Your clarification now is very helpful because we frankly were not sure exactly how it was to be read.

Mr. WALGREN. The operative word, as I see it now, is "recommendation," as opposed to "review," and our purpose is to not be inflexible, anyway.

I would invite your response to the first question I asked about alternatives to the private accreditation. The question Mr. Weber raises about the cost is something that we are all very sensitive to and we are looking at any means to accomplish the same purpose.

Thank you very much, gentlemen; we appreciate your thoughts and very much appreciate your coming today.

STATEMENTS OF DALE F. SCHWINDAMAN, SENIOR STAFF VETERINARIAN, ANIMAL CARE STAFF, ANIMAL AND PLANT HEALTH INSPECTION SERVICE, U.S. DEPARTMENT OF AGRICULTURE, AND ROGER GERRITS, VETERINARIAN, AGRICULTURAL RESEARCH SERVICE, U.S. DEPARTMENT OF AGRICULTURE

Mr. WALGREN. The next panel is Dr. Dale Schwindaman, who is the Senior Staff Veterinarian of the animal care staff of the Animal and Plant Health Inspection Service under the U.S. Department of Agriculture. Dr. Schwindaman is joined by Dr. Roger Gerrits, an animal physiologist with the Agricultural Research Service of the Department of Agriculture.

Gentlemen, welcome to the committee. Your written statements will be made part of the record, as well as any other materials that you would like to submit. We would appreciate very much your comments and perspectives. Can we start with Dr. Schwindaman?

[The biographical sketch of Dr. Schwindaman follows:]

BIOGRAPHY

Dr. Dale F. Schwindaman

Dr. Dale F. Schwindaman, Senior Staff Veterinarian, Animal Care Staff, Veterinary Services, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Hyattsville, Maryland, was born and raised on a farm in Marysville, Kansas. He attended Kansas State University from 1947 - 1953 where he received the Bachelor of Science and Doctor of Veterinary Medicine degrees.

After attending college, he practiced for a short time in a dairy practice in Wisconsin, then spent 2 years in the Air Force as a veterinarian. In September 1953 Dr. Schwindaman began 2 years' service with the Livestock Sanitary Board in Minnesota, and in September 1957 began serving the Animal Disease Eradication Division (now Veterinary Services), USDA, holding such positions as District Veterinarian, Area Veterinarian and Assistant Veterinarian in Charge in New Jersey.

In January 1965 Dr. Schwindaman was appointed Veterinarian in Charge of Delaware, and in 1967 he was transferred to the Laboratory Animals Staff, Animal Health Division, in Hyattsville, Maryland, where he assisted in writing the regulations and standards under Public Law 89-544, Laboratory Animal Welfare Act; Public Law 91-579, The Animal Welfare Act; and Public Law 94-279, the 1976 Amendments to the Animal Welfare Act. While in Delaware, Dr. Schwindaman took postgraduate work in Animal Science and Animal Pathology at the University of Delaware. He assumed his present position of Senior Staff Veterinarian, Animal Care Staff, in March 1975. As Senior Staff Veterinarian, Dr. Schwindaman is responsible for the Animal Welfare Act and the Horse Protection Act.

Dr. Schwindaman is married, with three children who are in college, and resides in Rockville, Maryland. He is a member of a number of professional societies including the American Veterinary Medical Association and the National Association of Federal Veterinarians, of which he is a past president; D.C. Veterinary Medical Association; and the United States Animal Health Association. His interests include active participation in church work and community work. His favorite hobbies are fishing, woodworking, and camping.

Revised 10/7/81

Dr. SCHWINDAMAN. Thank you very much, Mr. Chairman. I understand that the committee has been advised that the Department of Agriculture did not have sufficient time to study the bill, and that we are here to answer any technical questions that you may have about the administration of the Animal Welfare Act. It is my pleasure to do that, Mr. Chairman, on behalf of the Animal and Plant Health Inspection Service, which has the delegated responsibility for enforcing the Animal Welfare Act.

Mr. WALGREN. Dr. Gerrits, is there any opening comment you would like to add?

Dr. GERRITS. Not at this point perhaps we should address questions to Dr. Schwindaman, first.

Mr. WALGREN. Well, perhaps I can just pose a couple of questions for discussion. Could you describe the present structure that APHIS currently has to deal with animal welfare?

Dr. SCHWINDAMAN. Yes, Mr. Chairman. In the Animal and Plant Health Inspection Service we have a division of responsibilities, staff responsibilities and line responsibilities. My responsibility is staff function—to support the lines enforcement of the Animal Welfare Act. We have five regional offices headed by regional directors who are veterinarians, and a field force directed by veterinarians in charge, or officials in charge of each State. The officials in charge of each State have people in the field who make the actual inspection under the authorities of the Animal Welfare Act.

Now, relative to the research facilities, the inspections are made by veterinary medical officers; this is APHIS policy, whereas the other users of animals that come under the purview of the act can be inspected by either veterinary medical officers or nonprofessionals who are called animal health technicians.

Mr. WALGREN. I see. Can you give us some estimate of the number of people involved and how broad the ground of their jurisdiction is. Can they cover the field well, in your opinion?

Dr. SCHWINDAMAN. We feel that with the current organizational structure we have good inspection coverage of all of the licensees and registrants under the Animal Welfare Act. As far as the total number of people involved in making inspections, we do not have an accurate account since the people that are in the field have other program responsibilities.

Mr. WALGREN. What kinds of additional responsibilities do they have?

Dr. SCHWINDAMAN. The Animal and Plant Health Inspection Service, Veterinary Services, the agency which actually has the responsibility for the Animal Welfare Act, has other disease control eradication responsibilities. Cooperative disease eradiction and control responsibilities, such as brucellosis, tuberculosis, cattle scabies and sheep scrapie, equine piroplasmosis, and many other diseases that affect the domestic farm animal population. These are some of the programs that the field people have responsibility for in addition to the Animal Welfare Act.

Mr. WALGREN. How has budget support been running for this particular line effort?

Dr. SCHWINDAMAN. You mean, Mr. Chairman, for enforcement of the Animal Welfare Act?

Mr. WALGREN. Yes, and this particular level of activity. Can you break out dollar amounts spent for the purpose of putting in place the people who are actually carrying out the inspections?

Dr. SCHWINDAMAN. Mr. Chairman, I can only speak to the Animal Welfare Act. The appropriation for fiscal 1982 was approximately $4.9 million, with which we will conduct approximately 80 man-years or 80 person-years of activity.

Mr. WALGREN. So we have 80 people for 1 year.

Dr. SCHWINDAMAN. Portions of a large number of people which will total 80 person-years.

Mr. WALGREN. I see. Are these just the people who are below the supervisor, State-by-State? Or do these 80 man-years that are invested include the supervisor?

Dr. SCHWINDAMAN. No, Mr. Chairman, you are correct, in saying that they are below the State supervisory level.

Mr. WALGREN. So, below the State supervisory level we have 80 man-years of effort, essentially.

Dr. SCHWINDAMAN. Yes, sir. That number includes the staff and the full-time people. We do have approximately 22 people in the field that are working full-time on animal welfare care activities in addition to the part time activity of each of the other field people. And that is what totals the 80 man-years.

Mr. WALGREN. It strikes me that it must be tough to cover all the institutions in the country with 22 full-time people.

Dr. SCHWINDAMAN. Mr. Chairman, the 22 full-time people do not cover all the institutions, that are licensed and registered throughout the country. These people have responsibilities such as monitoring the activities of other field people that are conducting inspections, making station reviews to assure that there is as much uniformity as possible in the inspection procedure, writing alleged violation cases and making some inspections.

Mr. WALGREN We are dealing with 22 full-time people and the additional help of some others which total taken together 80 people per year.

Dr. SCHWINDAMAN. That is correct, Mr. Chairman.

Mr. WALGREN. What is the budget request for fiscal 1983, for this level of the Department of Agriculture?

Dr. SCHWINDAMAN. The President's budget contained a request of $1.5 million for fiscal year 1983.

Mr. WALGREN. So that's a little better than one-fifth of the amount of money that you had before? And so we could expect if the administration is successful in giving the amount of effort that they feel is appropriate in that area, that there would be a major reduction in the number of man-years that you can allocate to that effort. Is that correct?

Dr. SCHWINDAMAN. That is correct.

Mr. WALGREN. Do you have any suggestions for how the enforcement of the Animal Welfare Act could be improved?

Dr. SCHWINDAMAN. Mr. Chairman, the Animal and Plant Health Inspection Service has done an in-depth review of the enforcement of the Animal Welfare Act and we have started a number of procedural changes and new initiatives in order to improve the enforcement even further. I might mention some of these, Mr. Chairman. One initiative is to have a national animal welfare advisory group

which would be comprised of representatives from the animal welfare organizations, the general public, the scientific community, the exhibitors, the other users of animals that come under the jurisdiction of the Animal Welfare Act. We are also revising a number of our internal policy memoranda to provide more specific and detailed instructions and interpretations for our field people who actually carry out the inspections.

We are also conducting additional training through the use of new audiovisual materials. One of the major improvements will be the development of new performance requirements for the people that are actually involved with making inspections. We're hopeful that the required adherence to new performance standards under the Civil Service Reform Act will provide a basis for uniformity, commitment and sensitivity to the animal welfare program. If we have some individuals who are not meeting these standards, although we do not really anticipate this, I feel that consideration will be given to taking some type of corrective action.

These are just some of the initiatives that are being developed at the present time.

Mr. WALGREN. Can you say how far along those plans are and when you feel that those initiatives would be in place and operating?

Dr. SCHWINDAMAN. We have every intention of having not only these, but additional initiatives and procedures in operation by the end of this current fiscal year.

Mr. WALGREN. In most governmental areas we really don't have the resources to cover the field the way we would like to. I think, in particular, of housing for senior citizens, where we are providing 60 units of housing in a community and there is a waiting list of a thousand people who would like to live in that housing. The same is true in almost every area of government.

How many man years would it take in your view, for you to be assured that you had a proper frequency of actual on-site inspection of all the institutions that are carrying out animal testing?

Dr. SCHWINDAMAN. Mr. Chairman, I think that is a question that would take some thought and analysis and I am sure that we would be very happy to provide the chairman with that information.

Mr. WALGREN. Thank you very much.

[The information follows:]

MAN YEARS TO ASSURE A SOUND FREQUENCY OF ACTUAL ON-SITE INSPECTIONS OF RESEARCH FACILITIES

A. Sound frequency of actual on-site inspections: 4 per year.
B. Number of man years: 25.

(1) Approximate number of research facilities (sites): 2,500.
(2) Average number of hours to inspect each site: 4.5 (1) × (2)=11,250.
(3) Annual frequency of inspections: 4 per year (1) × (2) × (3)=45,000 total man hours.
(4) Man hours per year: 1,840.
(5) Total man hours divided by man hours per year = 24.46 man years.

Mr. WEBER. Dr. Schwindaman, can you describe the experimentation that is going on for agricultural purposes in colleges and

universities today? I assume that your service has a great deal to do with that subject.

Dr. SCHWINDAMAN. I think Dr. Roger Gerrits would be in a better position to answer that question.

Mr. WEBER. Fine.

Dr. GERRITS. Thank you, Mr. Weber. Presently, the one point that needs to be made is the Animal Welfare Act, as it presently exists, includes six laboratory species and meat, milk, and egg producing animals are not included.

Dr. SCHWINDAMAN. Yes, that's correct.

Dr. GERRITS. I think that's an important point related to your question.

Mr. WEBER. I agree. Would you repeat that again?

Dr. GERRITS. The current Animal Welfare Act pertains to six species, laboratory species. This bill, if I understand it correctly, relates to birds and all mammals.

Mr. WEBER. All warm-blooded——

Dr. GERRITS. Yes. And I think that is a very important point to recognize in light of your question.

Mr. WEBER. If I understand you correctly, you are saying that the current Animal Welfare Act does not apply to cattle, sheep, and poultry? An effect of this legislation is the expansion of coverage to include those animals.

Dr. GERRITS. That is correct.

Dr. SCHWINDAMAN. Mr. Weber, if I may elaborate on that particular point. The authorities of the Animal Welfare Act include not only the six species that were initially covered in 1966, but all other warm-blooded animals as designated by the Secretary of Agriculture. At the present time, we do cover all warm-blooded animals with the exception—and this is by administrative policy—of birds, the laboratory rat, the laboratory mouse, and the domestic farm animals.

The definition of animal in the Animal Welfare Act does contain wording which, if the domestic farm animals were brought under, would provide a number of exemptions for farm animals that are used for specific types of research or studies.

Mr. WEBER. I see. Can you give us some examples of the types of experimentation on farm animals that would be regulated by the Federal Government with passage of this legislation?

Dr. GERRITS. Several areas of important research related to improving the efficiency of animal production could be incuded. We in USDA-ARS have not had an opportunity to review this bill in detail. After our initial reading, we do have several questions and concerns about the terminology used. From a scientific standpoint, this legislation is asking for information that cannot be measured on a clear-cut scientific basis. It becomes a matter of judgment of the people that are doing the review or inspection. Research with food producing animals often requires specific physiological, biochemical, metabolic and nutritional measurements to insure the health, comfort, and efficient production of food from animals. This legislation is not clear; however, there are a number of experiments related to farm animals that could be affected by this legislation.

Mr. WEBER. I see. Mr. Chairman, I don't have any further questions.

Mr. WALGREN. Just to clarify, Dr. Schwindaman. Going back to the 80 man-years, were those man-years strictly related to animal welfare or were they also involved with the additional responsibilities of disease control?

Dr. SCHWINDAMAN. No, sir. Those were strictly related to animal welfare responsibilities.

Mr. WALGREN. Thank you very much.

Gentlemen, we do appreciate your contribution. If you have any specific thoughts about the implications of this bill for agricultural animal use, we would appreciate having them within the next several days in order that we might evaluate them along with the rest of the testimony.

Also, if you would address your responses both to the committee and to Mr. Weber, I think that would be helpful, so that we can get them and deal with them as directly as we can.

Dr. SCHWINDAMAN. Thank you very much.

Mr. WALGREN. Thank you very much, and we appreciate your coming.

The last witness is Dr. Jules Cass, the Chief Veterinary Medical Officer with the Veterans' Administration.

Dr. Cass.

STATEMENT OF JULES CASS, CHIEF VETERINARY MEDICAL OFFICER, VETERANS' ADMINISTRATION, ACCOMPANIED BY GARY KRUMP, OFFICE OF THE COUNSEL, VETERANS' ADMINISTRATION

Dr. CASS. Mr. Chairman, I hope you will permit the presence of Mr. Gary Krump, who is a member of our Office of General Counsel in the VA.

Mr. WALGREN. We are very happy to have him here.

I don't know whether you have written statements at this point, but anything that you would like to submit in writing will be made part of the record. Please give us your perspectives in whatever way you would like to proceed.

Dr. CASS. Mr. Chairman, I am privileged that you asked me to appear before the committee and you to discuss the Veterans' Administration's experience with insuring proper care and handling of research animals. My position in VA is that of Chief Veterinary Medical Officer, Medical Research Service in the Department of Medicine and Surgery.

The VA has not been requested to develop a position on H.R. 6245. I cannot assure you, however, that we will ultimately support this measure insofar as it would appear to make the conduct of VA's research programs dependent on accreditations under the supervision of another Federal agency.

With your permission, I shall speak briefly of mechanisms initiated in VA that help fulfill VA's commitment to the humane care, treatment, and use of animal subjects in its research, development and education studies that contribute new knowledge and skills to improving the health care of veteran patients. I will then try to respond to your questions.

The five mechanisms instituted for helping fulfill VA's commitment to the humane care, treatment, and use of animal subjects in the research, technical development, and education training studies are as follows:

First. Subcommittees on Animal Studies of the Research and Development Committee are established at each VA local health care facility having programs of R/D/E involving animal subjects.

Mechanism No. 2. An "Approval Form for Animal Studies" requiring the signatures of the local health care facility staff or consultant veterinary officer, the chairman of the subcommittee on animal studies and the chairman of the research and development committee. This form properly completed must accompany each research proposal submitted for peer central VA review.

A third mechanism. A local and central VA process of veterinary medical specialist review of all animal-related matters in R/D/E study proposals.

A fourth mechanism. A nationwide policy of outside expert review and approval is maintained for each VA animal research facility and its operation.

And fifth. In the past we have had a nationwide program for training of VA animal research facility unit supervisors.

Prepared statements presented for inclusion in the record will provide details of mechanisms 1, 2, and 3. The mechanisms numbered 4 and 5 can be made available should the committee chairman so wish.

I shall try to answer questions regarding any of these mechanisms.

Mr. WALGREN. Thank you, Dr. Cass. Could you describe a little more in detail function 4, where you have an outside review of your facilities. What does that entail?

Dr. CASS. The Veterans' Administration considered when reviewing the animal welfare law that although Federal agencies were made responsible for their own surveillance, whether or not the in-house use of our veterinary medical staff people for inspections of that kind would suffice or whether to commit us—various institutional groups to the visitations of the AAALAC which is the only accrediting body presently operating in the nation in this area. It was determined that we would contract for the services of the AAALAC and initiate a program of repeated visitations for accreditation through that institution. This has been going on and as of today 80 percent of VA's research facilities where animals are being used are fully accredited and the remainder are very well on their way to achieving this. Many of them have been revisited in the 3-year cycle that has been set up, and some of them have been visited coming on to the third time. In fact, we have had the program going that length of time.

Mr. WALGREN. What's the relationship of the 20 percent that are not, as I understand it, fully accredited——

Dr. CASS. The basis for this?

Mr. WALGREN. No, my instinct would be that AAALAC visits those facilities and comments on them, is that correct?

Dr. CASS. I receive a copy of the letter that goes to the institution so that as the Chief Veterinary Medical Officer I can be aware of the deficiencies. And I am aware of the deficiencies as well as the

suggestions and recommendations which also accompany these reports back to the hospital.

And we are aware of the actions that are taken by these facilities because generally these are related to funds needed for space, for equipment, and even for staff in some instances. Many of the corrections can be done and are done at the local level and those that cannot be handled principally where funding is concerned, we learn of those very shortly after the visits occur.

One of the practices that the AAALAC has is requiring an annual report from the institution that had been visited to learn whether or not there are any changes that are significant in the operation of the facility that must be brought to the attention of the accrediting body and also what is being done about the deficiencies and/or suggestions. This is required annually.

Mr. WALGREN. Very interesting. So, as I understand it, for these laboratories in the 20 percent that aren't accredited, this is what happens. There is a visit that is an onsite evaluation carried out by AAALAC. AAALAC then writes a report of each nonaccredited lab or facility. AAALAC writes a report citing or specifying whatever deficiencies they find and then that report is distributed both to the facility and also to those in charge of supervising the organization.

Dr. CASS. The report is directed to the director of the hospital or the facility and——

Mr. WALGREN. But that does come to you, also.

Dr. CASS. A copy of that does come to my office, yes.

Mr. WALGREN. And that report states the deficiencies that were found?

Dr. CASS. As well as suggestions for improvement.

Mr. WALGREN. As well as suggestions for improvement?

Dr. CASS. Yes.

Mr. WALGREN. And then there is a yearly response of the institution as to their progress, if any, in satisfying those deficiencies?

Dr. CASS. Correcting the deficiencies. By writing precisely what they have done, some have been taken from what is called a provisional status or a probational status. The AAALAC has a process whereby they review these letters and may even determine without another site visit that the matter has been taken care of and they grant full accreditation. This isn't done casually; it is done in a council meeting of the representatives of the AAALAC. They may on the other hand decide, and this is strictly up to AAALAC, and its governing body, its council and board, that things don't look well and they have heard this, that, or the other thing by way of whatever means. And they will ask to make another site visit within that 3-year period.

Mr. WALGREN. It seems like a pretty effective way to call to the attention of whoever is responsible for a facility exactly what the circumstances are in that laboratory, both physical and care-wise.

Dr. CASS. It has its drawback in one respect. Because it is not law, these standards are of the guide that HHS has supported and brought together by a select committee at the National Research Council for its preparation. If the site visit finding is marginal, that is to say if it does, in fact, not have any remarkable deficiency, and yet the suggestions may be a lengthy suggestion list, those who

mentally hold higher standards in this matter may ask, "How in the world did that particular facility gain accreditation when things are the way they are?" Well, in fact that is a comparative, judgmental matter and may give rise to a general feeling that AAALAC is being lax, whereas what it is is that there is an acceptable floor of humane care that the accrediting body must relate to, and a floor of what constitutes an acceptable and not deficient facility and operation.

Mr. WALGREN. Maybe you could tell us of your experience on two counts. AAALAC accreditation would cost in two ways, as I understand it. You would have a yearly cost for this outside service. AAALAC doesn't do this for nothing, I imagine. The VA in incurring that cost, apparently has decided that it is a good investment of that money on a year-by-year operating basis. Then the second level of cost would be in bringing your facilities into compliance. I gather there has been a growing percentage of your facilities that are in compliance. What has been your experience in both those areas of cost?

Dr. CASS. Well, the cost for outside service has risen. Costs per hospital unit have risen because of inflation and costs of sending site visitors out and costs of bringing them together to discuss the results of the visit and to determine the status of each one of these hospitals. So that this has moved up over the years necessarily, although one must be aware that the AAALAC is a nonprofit organization. That is a rather minor cost, if you will. The truly costly area is preparing facilities so that they may gain and sustain accreditation. That cost has skyrocketed and becomes a very formidable amount of money. When one could previously talk about a $25,000 renovation, that has moved up to a $250,000 renovation. The cost per square foot of animal research facility or animal facility has gone from where we could talk, and I am speaking now over a period of 15 years, of increases going from approximately $30 to $50 a square foot to $165 to $170 a square foot. And you can't cut corners on it because these are units that require special, very expensive air handling matters, and require equipment installed that do what we want to have done from the operational standpoint, for the humane care, treatment and use of these animals. That is a very expensive aspect.

Mr. WEBER. Mr. Chairman, would you yield?

Mr. WALGREN. Yes.

Mr. WEBER. Dr. Cass, have you made any projections of the costs required to bring the remaining 20 percent of the facilities, that are not currently in compliance, up to standards?

Dr. CASS. We can do better than projections on most of these because most of them have already been planned and are on their way. I don't have the figure in my head but we are talking millions.

Mr. WEBER. Millions.

Dr. CASS. Yes.

Mr. WEBER. Dr. Raub cited a figure for upgrading other facilities nationwide of one-half billion dollars. With your knowledge of what it has cost to bring your facilities into compliance and what it will take to bring the remainder into compliance, do you think his forecast is reasonable?

Dr. CASS. It is reasonable, absolutely.

Mr. WEBER. You do not believe that's an inflated figure?

Dr. CASS. No. As a matter of fact, wait until tomorrow and it will be larger. It is moving that rapidly.

Mr. WEBER. Thank you, Mr. Chairman.

Mr. WALGREN. Can you give us some indication of the benefit that the VA has received from moving in this direction? In other words, you obviously didn't incur these costs because you wanted to; at some point the VA decided that this was the right way to go. Could you give us your experience and your feelings for the justification of going in that direction?

Dr. CASS. There are at least two benefits that come from the activity and the investment. No. 1, certainly an awareness that there is a responsibility in the VA for the animals that are being used in that program. Providing the kind of facilities that tend to lessen the opportunity for problems to arise is one of the basic reasons for VA moving in the direction that it did.

Second, providing facilities and their operation for animal subjects that contain fewer variables has assisted the investigators in their research product in that when they designed a particular study, and the aims of the study were particular aims, there is less likelihood of confounding the results or compromising the results when the animals are stabilized, healthy and if I may use the word, normal acting.

So that it benefits the well-being of the animal and the responsibility that VA has to the presence of the animal and it benefits the product of research using animals.

Mr. WALGREN. Would you care to comment about the form that you are using for peer review. This was point No. 2 of the five mechanisms you mentioned in your statement, that VA has initiated to help fulfill its commitment to humane care of animals.

Dr. CASS. Well, the form is a form that is filled in by the investigator. I have given a copy for the record so that you have it to review in detail. It is a form that states very clearly, as a checkoff, that, one, the study is properly planned, carried out and terminates with due and acceptable regard for the welfare of the animal subjects.

Second check space, the study designed and conducted to avoid inflicting pain and/or suffering, including the appropriate use of tranquilizers, analgesics, and anesthetics.

A third check box, adequate safeguards for the safety and comfort of the animals in conformance with all pertinent animal welfare laws, regulations, and policies.

Another box, adequate safeguards against sources and introduction of potentially biohazardous agents or substances into or from any population in the environment outside of the study design. For example, the escape or presence of a noxious agent, radiation, viruses, adverse biologically active chemicals, or dangerous species or variance in the surroundings of the animals.

And the last, the biomedical appropriateness of the proposed use of the selected animal model, especially those endangered or threatened with extinction.

The local subcommittee on animal studies receives this and they sign—this is a collective judgment. They either approve and recom-

mend that the statements are true in their judgment or disapprove for reasons stated in the attached memorandum, or approve contingent upon making changes stipulated in the attached memorandum. This is signed by the chairman of the Subcommittee on Animal Studies, as well as the Veterinary Medical Officer. This, in turn, goes to the local Research and Development Committee, where the Chairman must sign off as approved or disapproved.

The Chairman of the Research and Development Committee, which is the parent committee, cannot approve the form that is disapproved for whatever reason until changes are made and the Subcommittee on Animal Studies does approve it. It can't be washed over, so to speak.

This form comes in with any animal protocol requesting funding and approval in our central review. If it is not present, it is requested specifically.

Mr. WALGREN. I see. Thank you very much, Dr. Cass. We certainly appreciate your perspectives. If there is anything further that you feel we should take account of, or amplification of any of the things you have said, we would like to have it for the record. Any written submission you would like to make would be most welcome.

Dr. CASS. Thank you.

Mr. WALGREN. I don't want to put you to extra work. But if, as you think back over the ground that you have heard covered and that you have covered this morning, there is something you feel we ought to take account of, we would certainy appreciate knowing about it.

Dr. CASS. I would only make one additional remark, if I may, Mr. Chairman. VA has its own sized animal research facility units. And the number of research studies that are conducted in these units are from maybe one study at an institution to several hundred at the large institutions. This is in no way comparable with many of the academic institutions or commercial institutions that have animal studies. And I think this must be taken into consideration when one looks at the mechanisms that we have installed and are operational as compared to institutions that are not sized, as ours.

Mr. WALGREN. I see. Thank you very much. And we will keep the record open for any other statements by Members of Congress who may wish to add them to the record.

[The information submitted for the record by Dr. Cass follows:]

GUIDE FOR VETERINARY MEDICAL SPECIALIST PANEL FOR MERIT REVIEW OF ANIMAL RESEARCH PROTOCOLS

A. Purpose of the Written Veterinary Medical Review:

1. An appropriately completed and signed Veterans Administration Animal Study Project Approval Form (VA-10-4785) generally assures that a particular proposal includes sound, acceptable animal medical and husbandry practices in Animal Research Facilities that are operated in conformance with all pertinent animal welfare laws, regulations and policies. This form, properly executed, must accompany each proposal involving animal subjects.

2. The Veterinary Medical Reviewer calls attention to and/or questions the absence or inadequacy of animal-related research details he/she considers to be essential in carrying out the specific design and aim(s) of the particular animal research project. He/she critically evaluates in particular animal-related research considerations that are described in and are necessary for the specific proposal write-up.

B. Coverage of the Written Veterinary Medical Review:

1. The written design and aim(s) of a specific animal research proposal is evaluated by the Veterinary Medical Reviewer for adequacy, inadequacy or omission of the following considerations:

a. Brief Description of Animal Component(s) in Protocol- Briefly, what species of animal(s) is to be studied as a model or system for what purpose
b. Animal Model

(1) Identifies specifically named; species; strain; age; sex; size; and number.

(2) Determines if the investigator justifies the appropriateness of the model for the specific, proposed use (through literature or documented personal experience).

(3) Questions use of animal subjects that are difficult to obtain or threatened with extinction.

(4) Identifies the appropriateness of specified animal source(s) (commercial, private, produced in VA Hospital, through VACO agreement(s) or contract(s).

(5) Determines whether investigators has had experience (extent) with the proposed animal model system or with the animal techniques and procedures proposed (publications, preliminary data).

(6/27/79)
JC (151E)

SEE New Examples of Written Reviews.

C. Biological and Medical Definition of Animal Model:

1. What feature(s) and or characteristics must the animal model possess or not possess in order to serve the aim(s) of the specific proposal: anatomic; physiologic; genetic; microbial; parasitic; pathologic; behavorial?

D. Environmental and Experimental Animal-related Factors:

What particular factor(s) and or conditions are essential to the design and aim(s) of the specific proposal; what essential factors are lacking in the write-up, the following among others:

1. Surgical study setting; barrier system setting (containment, exclusion); radioisotope setting; physical, chemical (including nutrition) and biological factors in the setting; experimental study design factors in the setting (sample size, animal subject numbers, randomization of factors in the study setting); procedural factors in study setting (surgical and nonsurgical techniques, use of devices); safety factors in the study setting (oncogenic, microbial, chemical, radioisotopes).

2. Is there evidence presented in the protocol (preliminary study, publications) of adequate experience with the proposed technology of manipulation, monitoring and measuring?

3. Can the use of the intact animal and/or its parts be extended beyond this particular proposal for purposes of other humanely and scientifically compatible studies by the proposing principal investigator and/or others (example: a proposal requiring only the use of a kidney or eye of many animal subjects for an in-vitro study)?

4. If painful procedures are involved, can they be avoided or is their management satisfactorily described?

E. Budget:

Animal-related auxilliary research personnel support (biological lab animal aids, technicians, technologists); animal husbandry, monitoring, restraint and barrier equipment; animal study and maintenance space; animal-related supplies; animal subject costs itemized, including: procurement, transportation, conditioning and maintenance per diem charges, from delivery to disposal.

F. Veterans Administration Approval Form:

For each Animal Research proposal, properly completed and signed. (Concurrence by Hospital's Chief or Consultant Veterinary Medical Officer).

(5) Any alternate courses of action open to the subject — generally another accepted course of therapy or diagnostic procedure — in lieu of participation in the study.

(6) A statement that the subject may withdraw without prejudice at any time from participation.

B. If it is determined that a Human Participation Statement is not required for an HSR&D proposal, please include a sentence here explaining this decision.

Animal Subject Statement

Animal research proposals will not be reviewed until they have been approved by the local Subcommittee on Animal Studies. Each submission must contain, with Veterinary Medical Officer concurrence, a completed VA Form 10-4785, Approval Form for Animal Studies. Each proposal must also include the following explicit, animal-related information.

A. Specify and justify the appropriateness of the species, strain, age, sex, size and number of animal subjects. Include evidence (pilot study, publication(s)) of experience with the specific technologies of manipulation, monitoring and measuring the proposed animal model(s).

B. Identify the source(s) of each proposed animal model.

C. Biological and Medical Definition of Animal Model(s):

1. Specify those biomedical characteristics that the proposed animal model(s) must possess, lack or have controlled or eliminated in order for the investigator to carry out successfully the design and aims of the particular proposal. (Such characteristics are: anatomic, physiologic, genetic, microbial, parasitic, pathologic and behavioral).

2. Where essential to a particular proposal, describe screening procedures for selection of and the conditioning regimen for the animal subjects.

D. Experimental and Environmental Factors:

1. Identify the availability or need for trained ARF personnel, space, devices and instruments for: surgical study(ies); barrier systems (containment, exclusion) study(ies); radioisotope study(ies).

2. Define the proposed management of essential physical, chemical and biological factors (including nutritional and hazardous substances) in the study.

3. Where essential to a specific proposal, indicate:

a. Sample size and frequency; animal subject numbers; randomization of the animal-related factors (the numbers housed together, the position of animal on cage rack, etc.).

b. Surgical and non-surgical manipulation and monitoring techniques, use of devices.

c. Regimen for managing unavoidably painful procedures (surgical and non-surgical), including appropriate use of anesthetics, analgesics and tranquilizers.

Privacy of Information Statement (for HSR&D proposals)

Due regard for Public Law 93-579, The Privacy Act of 1974, should prevail and evidence of intent to comply should be explicitly presented in this section. A statement from the facility Privacy Officer (usually the Chief, Medical Administration Service) should be included.

Biohazard Statement

Any program that contains procedures that constitute a potential or possible biohazard must either be accompanied or followed within 30 days of the deadline for submission by an explanation of safety precautions to be taken. A statement of the local VA or university biohazard committee must also be submitted within the same time constraints.

PRIVILEGED INFORMATION

VETERINARY MEDICAL
REVIEWER'S REPORT

TAB NO._____
MRB_____
DATE_____

VA Facility:
Principal Investigator:

NOTE: Dr. may wish to discuss the following animal related matters with the Medical Center's Veterinary Medical Officer.

1. DESCRIPTION OF ANIMAL COMPONENT(S) IN PROTOCOL:

2 Animal Model(s)

3 Biological and Medical Definition of Animal Model(s):

4 Environmental and Experimental Animal-Related Factors:

5 Budget:

✓ 6 Approval Form For Animal Research Proposals (see below)

(Prepare with spacing above Items 1 - 5 as warrented by each proposal)

SIGNATURE:

6. Approval Form for Animal Research Proposal(s):
Completed and appropriately signed ☐ Incomplete ☐
Inappropriately signed ☐ Absent ☐

VA Form 10-7962
JUNE 1977

Supersedes VA Form 10-7962, Dec 1976 which will not be used.

APROVAL FORM FOR ANIMAL STUDIES		DATE
VA FACILITY	PRINCIPAL INVESTIGATOR	MRIS NO.

DESCRIPTIVE TITLE OF PROJECT (*Procedure, study, etc., attached.*)

ATTACHMENT # 2

This "Approval Form for Animal Studies" appropriately completed and signed, with written concurrence of the hospital's staff or consultant Veterinary Medical Officer. This ordinarily gives assurance: that a particular animal research proposal includes sound, acceptable Veterinary Medical care, nursing and animal husbandry practices carried out in facilities operated in conformance with all pertinent animal welfare and safety laws, regulations and policies.

This is to certify that the Project, identified above, has been reviewed by the Research and Development Committee's Subcommittee on Animal Studies, specifically considering the following:

☐ a. The study is properly planned, carried out and terminates with due and acceptable regard for the welfare of the animal subjects.

☐ b. The study designed and conducted to avoid inflicting needless pain and/or suffering - including the appropriate use of tranquilizers, analgesics and/or anesthetics.[1]

☐ c. Adequate safeguards for the safety and comfort of the animal subjects, in conformance with all pertinent animal welfare laws, regulations and policies.[1]

☐ d. Adequate safeguards against sources and introduction of potentially biohazardous agents or substances into or from any population(s) in the environment, outside of the study design (example: escape or presence of a noxious agent - radiation; oncogenic virus; adverse, biologically active chemical; dangerous species or varient, etc.).

☐ e. The biomedical appropriateness of the proposed use of the selected animal model, especially those endangered or threatened with extinction.[2]

SUBCOMMITTEE ACTION

THE COLLECTIVE JUDGEMENT IS:

☐ APPROVAL IS RECOMMENDED. ✓

☐ DISAPPROVAL FOR REASONS STATED IN ATTACHED MEMORANDUM.

☐ APPROVAL CONTINGENT UPON MAKING CHANGES STIPULATED IN THE ATTACHED MEMORANDUM.

DATE OF ACTION

(SIGNATURE)
Chief or Consultant Veterinary Medical Officer

(SIGNATURE)
CHAIRMAN, SUBCOMMITTEE ON ANIMAL STUDIES

RESEARCH AND DEVELOPMENT COMMITTEE ACTION

☐ APPROVED

☐ DISAPPROVED

☐ RETURNED TO SUBCOMMITTEE FOR FURTHER ACTION

DATE OF ACTION

(SIGNATURE)
CHAIRMAN, RESEARCH AND DEVELOPMENT COMMITTEE

[1] VA Publication IB 15-12, April 1975, "Synoptic Guide to Animal Welfare Laws, Regulations and Policies Governing Biomedical Facilities and Programs Involving Animal Subjects in VA Hospitals.

[2] Questions regarding endangered animal species or those threatened with extinction should be directed to VACO's Chief, Veterinary Medical Officer (151E).

VA FORM FEB 1977 10-4785

PRIVILEGED INFORMATION

VETERINARY MEDICAL
REVIEWER'S REPORT

TAB NO._____
MRB_____
DATE_____

VA Facility:
Principal
Investigator:

NOTE: Dr. may wish to discuss the following animal related matters with the Medical Center's Veterinary Medical Officer.

1. DESCRIPTION OF ANIMAL COMPONENT(S) IN PROTOCOL:

SIGNATURE:

Approval Form for Animal Research Proposal(s):
Completed and appropriately signed ☐ Incomplete ☐
Inappropriately signed ☐ Absent ☐

VA Form 10-7962
JUNE 1977

Supersedes VA Form 10-7962, Dec 1976 which will not be used.

PRIVILEGED INFORMATION
VETERINARY MEDICAL REVIEWER'S REPORT
Continuation Page

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VETERANS ADMINISTRATION
Washington, D.C. 20420
November 18, 1977

INTERIM ISSUE 10-77-46

A. BASIC ADMINISTRATIVE ISSUE AFFECTED: M-3, Part I, Chapter 1.

B. OTHER ISSUE AFFECTED: M-3, Part II, Chapter 1; Interim Issue 10-75-8.

C. REASON FOR ISSUE: To establish the membership of the Research and Development Committee and to define its functions and responsibilities. Subcommittee on Animal Studies. (see pp. 3,4)

D. TEXT OF ISSUE:

1. The Research and Development Committee is responsible through the Chief of Staff to the facility Director who appoints its members.

a. In facilities affiliated with academic institutions, the membership consists of representatives from each of the following groups:

(1) At least one but not more than three members from the affiliated institution as representatives of the Deans Committee. When two or more medical schools are affiliated with the facility, their representatives collectively shall not exceed four members in total.

(2) At least two but not more than four members from the staff of the facility, selected because they have major patient care or management responsibilities. Preferably, they should have training and experience in research as well.

(3) At least one but not more than three members who are Veterans Administration (VA) employees, selected because they are actively engaged in major research or development programs or can provide research or development expertise. They may hold appointments in the VA Career Development Program.

(4) Whenever possible, one member of the Committee selected according to the criteria listed above should have expertise in biostatistics and research design and another in animal research techniques and biomedical study settings. The members should have diverse backgrounds and include at least one non-physician.

(5) Ex Officio members are the Director and Chief of Staff and the Administrative Assistant to the Associate Chief of Staff for Research and Development of the facility, without vote, and the Associate

c. The minutes of the meeting will be signed by both the Chairperson and the Executive Secretary. Copies will be submitted to the facility Director, the Chief of Staff and the Clinical Executive Board for review.

d. Within three weeks after the meeting, copies of the minutes, together with any comments the Director cares to make, will be distributed to all members of the Committee and made available upon request to any investigator.

e. Within three weeks after the meeting, two copies of the minutes for that meeting will be forwarded through appropriate channels to the Associate Deputy Chief Medical Director for Operations (15C).

5. Subcommittees of the Research and Development Committee are established by that Committee, the members being nominated by the Committee and appointed by the facility Director. Each Subcommittee will keep minutes of its meetings and reports to the Research and Development Committee which accepts or rejects its recommendations, except that the parent Committee cannot alter an adverse report or recommendation of the Subcommittee on Human Studies or the Animal Research Subcommittee when either recommends disapproval for ethical or legal reasons. The subcommittees include:

a. Subcommittee on Human Studies, members of which serve for terms not to exceed three years on staggered appointments.

(1) Its membership must include:

(a) A Chairperson who is a VA employee, with or without compensation.

(b) Two or more members who are neither VA employees nor directly connected with research and development within the VA facility. These members appropriately include a member of the clergy, lawyer, representative of a legally recognized Veterans' organization, or practicing physician from the community.

(c) Such additional members as will enable the Subcommittee to consider the ethical and legal issues involved in the participation of human subjects in research and development.

(d) The membership must fulfill relevant legal and regulatory requirements of the VA, Department of Health, Education, and Welfare, and of other Governmental agencies.

(2) The facility can use a comparable "human rights committee" in lieu of the Subcommittee on Human Studies, providing the committee

includes among its membership representation from VA staff salaried more than half-time by the VA. Generally, this will be constituted by an affiliated medical or dental school or by another VA facility. The Research and Development Committee of a facility must assure the Director in writing that the outside committee in structure and function conforms to or exceeds the requirements for a Subcommittee on Human Studies. This assurance must be reaffirmed annually after review of the Committee's structure and performance.

(3) The Research and Development Committee retains the responsibility to review and concur with the recommendations of the Subcommittee that is used, but cannot alter or reject an adverse report.

b. Subcommittee on Animal Studies in any facility that has animal activities.

(1) Its membership will include:

(a) At least one member of the parent Research and Development Committee.

(b) A Veterinary Medical Officer who is a VA employee, with or without compensation, and who serves ex officio, with vote.

(c) Total membership will include two to four VA investigators who are involved significantly in studies using animal subjects.

(d) Members other than those who are ex officio serve terms not to exceed three years on staggered appointments.

(2) The Subcommittee on Animal Studies will be responsible for reviewing all use of animal subjects at the health care facility. Review will include all newly proposed and ongoing studies, as they relate to any pertinent animal welfare laws, regulations, and policies. Such studies will be reviewed for the appropriateness, quality, and availability of the selected animals; for the humaneness and appropriateness of procedures; and for the appropriateness and humaneness of conditions surrounding animal subjects before and throughout the study. This review includes assessment of adequacy and availability of essential animal research facilities support.

(3) The Subcommittee on Animal Studies will evaluate, at least annually, the animal research facility to identify deficiencies relevant to any pertinent animal welfare law, regulation, or policy. The Subcommittee will recommend appropriate actions to correct deficiencies determined in this evaluation, and will report on corrective measures taken.

c. Research Equipment Subcommittee in any health care facility with a large or complex research program.

(1) The membership should include a biomedical engineer if available to the facility, a basic scientist, the Administrative Assistant to the Associate Chief of Staff for Research and Development, and one or more investigators having a broad knowledge of research instrumentation.

(2) The Research Equipment Subcommittee will be responsible for evaluation of all research equipment requests and for recommending to the Research and Development Committee whether the equipment requested is fully justified and documented. For each request, the Subcommittee will determine whether an alternative piece of equipment is available or could be made available, and whether the equipment requested is optimal for the purpose proposed.

(3) The Research Equipment Subcommittee will periodically report to the Research and Development Committee on equipment utilization at the health care facility. This report will specifically discuss current actual utilization, potential for sharing within the facility, and the need for disposal of equipment.

d. Such other subcommittees as are deemed necessary by the Research and Development Committee. Each Subcommittee will have at least one member from the parent Committee.

6. A facility which has a limited research and development program may use the Research and Development Committee of another VA facility to advise the Director.

a. The Director of the facility may arrange for assistance from the Research and Development Committee of another facility through the Director of the Medical District and the facility Director or may request the assistance of the Assistant Chief Medical Director for Research and Development through appropriate channels. In any event, he/she should notify the Assistant Chief Medical Director for Research and Development of the arrangement.

b. The Chief of Staff or Coordinator of Research and Development of the facility requesting assistance is responsible for providing such documents and other support as the cooperating Research and Development Committee needs to render assistance.

7. The Research and Development Committee is responsible through the Chief of Staff to the facility Director for maintaining high standards throughout the facility's research and development program. These standards include those concerning the scientific quality of

E. COMPLIANCE: Facility Directors will implement changes required by this Issue in an expedient manner so as to be in full compliance as soon as possible, but not later than March 1, 1978, except for the membership of the Human Studies Subcommittee previsouly established in Interim Issue 10-75-8 and in effect at this time.

F. RECISSIONS: M-3, Part I, paragraph 1.06c (3), 1.07 and 1.21 g, h and i (as added by Interim Issue 10-75-8); M-3, Part II, paragraph 1.07e (2) and (3). This issue is rescinded November 10, 1978.

JOHN D. CHASE, M.D.
Chief Medical Director

Distribution: RPC: 1041
FD

EXAMPLE WRITTEN REVIEW

1. Animal Component(s) in Proposal:
The effects will be studied of an Acetosalicylic acid, anti-histimine (unnamed), Dextran 40 and 70, sterile saline and heparin on adhesions induced in rats by means of a surgically induced peritonitis. Mechanism(s) of effect are purported to be an aim of this proposal.

2. Animal Model:

a. 132 (Phase I-IV pp. 17-21) male Sprague-Dawley rats 250-350g. (although budget page requests 350 rats - is this in part to account for the 25% mortality experienced with the induction of peritonitis?) procured from Harlan Industries, Indianapolis, Indiana.

b. P.I. has had a pilot experience with using mini doses of heparin in the rat peritonitis model leading to 1 publication, Ref. 23, pg. 7.

c. This peritonitis rat model is cited in several refs. in bibliography that is missing in this proposal.

3. Biomedical Definition of Animal Model:
Essential need is for procuring and maintaining rats free of known diseases particularly enteric pathogens. Recommend procuring rats through the VA-NCI agreement, Circular 10-78-268, November 22, 1978.

4. Experimental and Environmental Animal-Related Factors:

a. Proteus spp. are commonly present in drinking water and, in debilitated post-op rats, these organisms can become important pathogens. The hospital's Veterinary Medical Officer, [redacted] can advise in this matter.

b. The "Animal Subject Statement" pp. 11-14 is a lengthy discussion of animal matters that do not focus at all on the essential needs of the specific design and aims of this protocol, (for example: will various body surface

and exteraneous organisms be kept out of the surgery by the use of sterile surgical techniques; will there be any necessary pre and post surgical support regimen that would more closely resemble the human surgical condition in peritonitis and others as in paragraph 4 of this review). The Animal Studies Approval Form appropriately completed and signed is the declaration that the ARF is designed and operated in accordance with the animal welfare laws, policies, etc., and does not require any elaborated statement except as some additional element in the scientific judgement of the P.I. bares essentially on the success of this study. Such essential animal related matters should be discussed at the appropriate point in the body of the protocol.

c. It is totally unacceptable to combine the surgery or the kitchen with the necropsy space (pg. 12) in animal research. A small HEPA filtered unidirectional air flow plastic tent over a surgical surface could be designed for use in a multipurpose animal procedural lab or in an animal ward containing physiologically stabilized members of the same species. Discuss with the hospital's Veterinary Medical Officer. Scheduled use of the ARF surgery should be considered.

d. Since peritoneal microbiological flora will be cultured, need is for a sterile surgical technique.

e. Need is for a stated pre surgical management of diet preparitory to inducing the peritonitis.

f. Need is for a stated post surgical regimen of medical and nursing care by trained ARF personnel as required by and in support of the design and aims of this particular proposal.

g. No dosage is given for administering any of the control or test agents. Concentration, and total amount of each of these agents are critical and need to be fully justified before any measurements of effect can be undertaken.

h. Anesthetics are named only on the budget page 3. No dosage for nembutal is given and ether, if justified and necessary, presents a safety hazard. No acceptable method of destroying the rats is given.

i. Approval by the Radiation Control Committee (pg. 17) is not present and should have been submitted at the time of submission of this proposal.

j. It will be surprising if distribution patterns of ip injected agents in peritonitis models are uniform enough (with proposed small numbers of rats per group) to permit conclusive comparisons.

k. 25 percent mortality in untreated peritonitis induced animals ought to be reduced before proceeding with the definitive study. Consider preparing a 1 cm pedicle of ileum, instituting a presurgical dietary management and, assuredly using rats free of known diseases (see para. 3a).

5. Budget:

a. Technician - no statement of what this technician will be doing. He should be experienced or trained in the animal-related science and techniques expected of him.	$11,505.
b. Animal subjects 300 rats [all 4 Phases of study proposal add up to 132 rats (even with 25 percent additional for mortality is 152 rats?)]	1,225.
c. Per diem rat maintenance (details are lacking to judge appropriateness)	178.

6. Animal Study Approval Form:
Present and appropriately signed.

EXAMPLE
WRITTEN REVIEW

1. Animal Related Component(s) of this Protocol:

a. Normolipidemic Swine will be studied to determine the effect of portal diversion, distal intestinal resection, distal intestinal bypass, the dynamics of lipoprotein, triglyceride and cholesterol.

b. Normolipidemic and nutritionally - induced hyperlipidemic rats will be studied to determine effects of portal diversion alone and combined with distal intestinal bypass on specific tissue cholesterol pools, in-vitro hepatic and intestinal cholesterol synthesis as well as in-vitro hepatic protein synthesis.

2. Animal Models:

a. 5 miniature male pigs, 20-40 kg, (Hampshire or Duroc), source unidentified.

b. 50 Holtzman rats, male or female, 250 gm, source unidentified. (Sprague-Dawley rats are designated on Animal Studies form).

c. PI has had experience with the procedures and has published successfully in the subject area. (Ref: (16 in prep., 19, 20, 21, 36 dog)(22, 59 rabbit) (32, rat).

d. Appropriateness of animal models: (1) swine - justification in the statement, without supportive literature or described personal data, that swine have an "analogous lipoprotein system" to man. - PI provides no evidence of experience with swine in the proposed study area although he presents a variety of swine studies by others (Refs. 25,26,27). (2) Rat- PI gives "cost" alone as the justification for use. He has published one paper (Ref. 32) and states findings of others using the rat as a model in various aspects of the subject area.

COMMENT: The PI has catalogued the various findings among a variety of animal species (including contradictory findings in many of the repeated studies by different investigators, including his own). Lacking, essentially, is the PI's synthesis and analysis of these disparate findings to give direct support to his selection of the animal models in this proposal and

provide confidence that his proposal will result in resolution of rather than adding to the already documented disagreements.

3. Biomedical Definition of Animal Subjects:

a. Need is for miniature swine and rats procured and maintained free of known diseases. Rats should be procured through the VA-NCI Agreement, Cir. 10-78-268.

b. Dr. should be able to locate a reliably defined source of miniature pigs.

4. Environmental and Experimental Animal-related Factors:

1) Unstated but needed is a planned regimen of pre and post operative medical, nursing and dietary care by trained ARF personnel to minimize the variable stress that can affect the results particularly at 7 day test period.

2) Although the studies involving 28 pigs are specifically designed for 24 months, there is no stated design for the 5 pigs budgeted in year one.

3) A sham control would appear to be just as necessary for the pig studies as for the rat studies.

4) How will the rats and pigs be destroyed, agent and dose? technique?

5) What specific diet will the pigs receive pre and post surgery? A "standard" diet does not describe this.

6) What size blood samples will be taken weekly from the heart of rat subjects and will this be done under anesthesia?

7) Radioisotopes ^{125}I and ^{131}I will be used in swine (noted in protocol writeup but not on animal use form).

5. Budget:

Animal subjects and maintenance:

a. 5 swine @ $130.00 each for 150 days @ 3.50/day $3,700.
How does the figure $3,700 derive of these calculations?

b. 50 rats @ 7.50 each for 40 days @ 0.09/day $ 600.

c. Surgical instruments $1,500.
Without details this figure cannot be judged.

d. No costs are included for animal transportation charges; for surgical table time; or for special diets to induce hyperlipidemia.

6. Animal Study Approval Form:

Present and properly completed.

EXAMPLE WRITTEN REVIEW

1. Animal Component(s) in Proposal:
Study 1. Rats administered tritium labeled 9, 10 palmitate bound to albumin (DPPC) (IV, tail vein) and lungs washed. Lavaged solution supernatant and sediment checked for radioactivity and each analyzed for disaturated lecithins and fatty acids.

Study 2. Lavaged solution (above) will be injected intratracheally into rats and destroyed at 5, 10, 20, 30 mins. and 1, 2, 3, 6 hours post injection. Aortic blood samples at death will be checked for radioactivity. Various body tissues will be held at - 50°C for "possible" later analysis? (pg. 4). These studies are to study the effect of macrophages on removal and/or degradation of surfactant.

2. Animal Model:

a. 300 Specific pathogen free Sprague-Dawley male rats Study 1. - 400± 100g; Study 2. -(wt. approx. 225 gms) procured from Hilltop Labs, Scotsville, Pa.

b. P.I. reports pilot study using 7 rats to establish the survival dose following injection of 0.5 - 1.0 ml of lavaged pulmonary fluid supernatant from radiolabeled DPCC injected donor and recovery from lavaged lung fluids of recipients (pg. 7 Table). He provides no other experience with this model or the techniques.

c. Use of the rat as a model in this subject area is quoted from a single Reference 8, pg. 9.

3. Biomedical Definition of Animal Model:

a. Need is for rats procured and maintained free of known diseases, particularly pulmonary infections such as mycoplasma and chronic viral pneumonia. The term pathogen

free rats needs to be checked for what pathogens this source of rats are free of.

b. Recommend that P.I. consider procurement of rats through the VA-NCI Agreement, Circular 10-78-268, November 22, 1978.

4. Environmental and Experimental Animal-Related Factors:

a. The column labeled "Radiolabeled fluid injected counts" is not clear (Table pg. 7).

b. P.I. reports no radioactivity in blood at death of rats in Study 2 (p. 8) possibly due to small sample size. He may wish to pool samples from 2 or 3 rats.

c. A laminar flow rack, appropriately used, is essential to this study. Maintaining 6 rats per week in laminar unit (pg. 12); will the newly received animals be maintained in a similar facility until used?

d. No statement is made regarding the handling and disposition of the radioisotope treated rats, unless para. 9 Appendix 1, pg. 9 application for use of radioactive materials is intended to cover this.

e. Rats in Study 1. - 30 mg/Kg Ip pentobarbital sodium used as anesthetic; whereas in Study 2 - 15 mg/Kg (pg. 4) Why? Is this an error?

5. Budget:

a. 300 rats - (see para. 3b, above) $2400.

b. No per diem costs noted for maintenance

c. 1 lab worker WG1- the animal maintenance and some of the animal handling support could better be performed by a trained ARF technician and funds requested to employ a part-time ARF trainee replacement. $5700.

d. Equipment - (1) Harvard rodent respirator $ 855.
(if this respirator is essential, how were the pilot tests (pg. 7) performed?)

(2) surgical supplies (Research Facilities available - pg. 14. - item 5 - includes surgical supplies) $ 800.

6. Animal Study Approval Form:
Present and appropriately signed. The title of the project is lacking.

WRITTEN REVIEW

1. Animal-Related Component(s) in Proposal:
The effect of sodium oxyferriscorbone (NaOFS) will be studied in preventing the formation of hemorrhagic gastric lesions induced in rats stressed by means of cold-restraint.

2. Animal Model:

a. 100 male Sprague-Dawley rats, 120-220gm will be studied. Source of animal subjects unstated.

b. The P.I. justifies this use of the rat as the "simplest and cheapest model" (pg. 102, Summary 5) and cites Ref. 57 "that NaOFS can prevent the formation of gastric ulcers in the rat after pyloric ligation." This reviewer also questions the relevance of this proposed rat model to the study of drugs in the treatment of gastro duodenal ulcer disease in man (see para. 3 below).

c. The P.I. has had experience and published using the proposed technique, and rats - Refs. 52, 53 (typo error Ref. 54, pg. 106).

3. Biomedical Definition of Animal Model:

a. There are other significant alarm responses of the stress syndrome inducing technique (Selye) the P.I. redeveloped that could affect the results. Although he reviewed the literature using various animal species and states in Summary (1) pg. 102 the pig is "the closest to the human and the best model", he rejects it on the basis of - cost and size (a non-research reason for selection) and selects the rat - which is "not fully representative of the chronic lesions that characterize duodenal ulcers, pg. 102". The P.I. also cites literature (Lifs 36, 37) stating pg. 99-3.2.2. that the ferret is a good basal secretor, sensitive to histamine and posseses intestinal morphology similar to man, where as the rat does not.

b. Need is for rats procured and maintained free of known disease, particularly gastroenteric parasites. Consider procuring rats through VA-NCI Agreement, Circular 10-78-268, November 22, 1978.

4. Experimental and Environmental Animal Related Factors:

a. Planned safe practice is required in the use of ether as an anesthetic and in disposition of the etherized carcasses.

b. Need is for stating the planned, acceptable method of euthanasia.

c. A 24 hour fast is undesirable for the rat, a 12 hour is adequate for the purpose.

5. Budget:

a. 150 Sprague-Dawley rats 150 (100 planned-pg. 105-5) @ $4 - No maintenance costs - per diem?	$600.
b. Equipment is appropriate	$119.
(1) Restraint cages (2)	
(2) Animal balance and operating boards	$130.

6. Animal Studies Approval Form:
Present and appropriately signed.

Mr. WALGREN. With that, I want to thank all the witnesses for coming today. Your comments and suggestions will be helpful to the subcommittee as we proceed with our work on H.R. 6245.

[Whereupon, at 11:10 a.m., the subcommittee was adjourned.]

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